A Longitudinal Investigation of the Psychological and Cognitive Sequelae of Liver Transplantation

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University of Edinburgh
1997

I declare that the work described here is entirely my own, except where I have acknowledged that of others.

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ABSTRACT

The psychological impact of chronic liver disease is vast, including the psychiatric and psychosocial consequences of chronic illness, and the cognitive deficits experienced due to hepatic encephalopathy. Orthotopic liver transplantation is now the treatment of choice for end-stage chronic liver disease, and it is now recognised that psychological factors play an important role in the evaluation of its outcome, as well as the more traditional measures of morbidity and mortality. Successful liver transplant recipients face a lifetime of drug regimens as well as the common psychological difficulties associated with transplantation, including fear of rejection and preoccupation with the donor. Preliminary findings have suggested that liver transplant recipients experience enhanced quality of life post-operatively compared to pre-transplant levels, although not at the level experienced by the general population. Investigation of the neuropsychological functioning of recipients has also produced mixed, although generally positive results. Much of the research in this field has, however, been methodologically flawed with the use of non-standardised measures, lack of control groups and retrospective, cross-sectional designs. Using a prospective design the present study aimed to investigate the effects of liver transplantation on neuropsychological functioning, psychiatric status and quality of life. Subjects were assessed pre-transplant and approximately three years post-transplant, as were a group of patients with liver disease not considered for transplantation and healthy controls. The roles of social support and self-esteem were investigated. The results were analysed and discussed. Limitations of the present study and implications for future research were identified.

CONTENTS

TABLES

ABBREVIATIONS

AIS	Acceptance of Illness Scale
ANOVA	Analysis of variance
CVLT	California verbal learning test
DF, DB	Forward and backward digit span subtests of Wechsler adult intelligence scale - revised
DSST	Digit symbol substitution test
EORTC	European Organisation for Research of Treatment of Cancer
HADS	Hospital anxiety and depression scale
HE	Hepatic encephalopathy
LC	Chronic liver disease controls
LHE	Latent hepatic encephalopathy
MMPI	Minnesota multiphasic personality inventory
MMSE	Mini-mental state examination
NART	National adult reading test
NHP	Nottingham health profile
NIDDKQOL	National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases Quality of Life form
OLT	Orthotopic liver transplantation
POMS	Profile of mood states
QoL	Quality of life
RAVLT	Rey adult verbal learning test
RBMT	Rivermead behavioural memory test
RSC	Rotterdam symptom checklist
RSE	Rosenberg self-esteem scale
SIP	Sickness and impact profile
SOS	Significant others scale
STAI	State trait anxiety inventory
TMT A	Trail making test A
Tr	Transplant recipients
VFT	Verbal fluency test
WAIS-R	Weschler Adult Intelligence test - Revised
WCST	Wisconsin card sorting test
WHO	World Health Organisation
WHOQOL	World Health Organisation Quality of Life scale
WMS-R	Weschler Memory Scale - Revised

ACKNOWLEDGEMENTS

There are many people that I must thank for making this work possible: my supervisors, Dr Ronan O'Carroll and Professor Mick Power; the transplant recipients, liver disease patients and the control subjects; Jill Cossar for her continual help; and the support throughout from Craig and my parents.

CHAPTER 1: INTRODUCTION

1.1. GENERAL INTRODUCTION

Liver transplantation involves major surgery, the possibility of many postoperative complications, and a lifetime of strict anti-rejection drug regimens. Nevertheless, it is the treatment of choice for end-stage liver disease and there are currently around 400 liver transplants undertaken in the United Kingdom every year, compared to less than 40 in 1981 (Price et al. 1995). The outcome of this treatment has traditionally been evaluated in purely medical terms. Interest in psychological factors is, however, growing. Neuropsychological impairment associated with liver disease, known as hepatic encephalopathy, has been well documented (e.g. Tarter et al., 1988a; Gammal & Jones, 1989). It has also been shown that the majority of patients suffering from chronic liver disease demonstrate cognitive impairment, often going unrecognised by doctors, known as latent, or sub-clinical hepatic encephalopathy (e.g. Tarter et al., 1990a; O'Carroll et al., 1991). It is assumed that successful treatment of the underlying liver disease would lead to a recovery of neuropsychological functions. A number of studies have used batteries of neuropsychological tests to investigate the outcome of liver transplantation. These studies will be discussed and evaluated. The role of alcohol abuse in this literature shall be discussed. Another major area of research in the field of liver transplantation is its outcome in terms of the quality of life of recipients, and an evaluation of the literature assessing quality of life shall be carried out. Adjustment to chronic illness can be a difficult process, involving the loss of roles and enjoyment of activities. Successful liver transplantation can restore many of these losses. Major surgery, and resulting complications and scarring have also been associated with adjustment difficulties. These issues will be discussed. The relationship between social support and health is complex, but adequate social support has been reported to be associated with good adjustment to illness, as well as a better health outcome. The role of social support shall be discussed,

although no studies have assessed this variable in the field of liver transplant research. Finally, the concept of self-esteem and its relationship to health shall be discussed. The aims of the present study will then be outlined.

1.2. The Liver

The liver plays an integral role in sustaining the nutritional and metabolic well-being of an individual: it determines whether to store or use immediately absorbed nutrients; it stores and activates several vitamins; it is involved in protein synthesis; it regulates the plasma level of cholesterol and other fats; it removes large cellular and protein foreign material from the circulation; and it manufactures bile. The obstruction of blood flow within the liver (portal venous obstruction) due to either cholestatic (obstruction of bile flow), or hepatocellular disease, results in hypertension and the shunting of portal venous blood around rather than through the liver. Thus the liver is no longer able to filter and metabolise portal venous blood constituents, and of particular interest to neuropsychologists, putative cerebrotoxins are not degraded and enter the systemic blood flow. This portal-systemic shunting of blood (which is also surgically induced to reduce hypertension) is the main cause of the complex neuropsychiatric syndrome known as hepatic encephalopathy (HE, Crossley & Williams, 1984).

1.3. Hepatic Encephalopathy

No strict definition of HE exists, although it is generally described as a potentially reversible metabolic encephalopathy, with augmented neural inhibition (Gammal & Jones, 1989). HE is usually categorised according to a rating scale devised by Parsons-Smith et al. (1957), which is a five point scale from 0 (no abnormality detected) to IV (coma). The earliest signs include psychiatric and behavioural changes and subtle changes in

intellectual function. Then motor function, intellectual abilities and consciousness become noticeably impaired, followed by coma. It has recently been discovered that the crude nature of this rating scale has masked subtle deficits. Many patients suffering from liver disease, who have no evidence of HE upon clinical examination, have significant neuropsychological deficits. This impairment, known as latent HE (LHE), or subclinical HE, is evident from neuropsychological testing (Conn & Lieberthal, 1978; Gilberstadt et al., 1980; Tarter et al., 1984). Macroscopic abnormalities of cerebral morphology have been demonstrated by CT scan abnormalities (Bernthal et al., 1987; Tarter et al., 1986a), NMR imaging (Moore et al., 1989). Finally, abnormal event-related potentials have been reported in cirrhotics without overt signs of HE (Kugler et al., 1992; Yang & Chu, 1985). It is generally agreed, however, that LHE is most sensitively assessed by means of neuropsychological testing (Tarter et al., 1989; Conn & Lieberthal, 1978; McClain, 1980). Furthermore, EEG investigations are normal in 66-94% of patients with LHE, and if abnormalities are detected on an EEG, more severe abnormalities are evident on neuropsychological testing (Rikkers et al., 1978; Schomerus et al., 1981; Gitlin et al., 1986; Dunk et al., 1988). There are a number of candidates for toxic factors that may be responsible for HE: ammonia; fatty acids; mercaptans; aminobutyric acid; plasma amino acid imbalance (Zeive, 1981; Schafer & Jones, 1982; Fischer & Baldessarini, 1971; James et al., 1979). No single hypothesis, however, accounts successfully for the development of HE in all patients (Lockwood, 1987).

1.3. 1. Neuropsychological Investigation

There is now a growing body of literature examining the neuropsychological sequelae of liver disease, and the use of extensive batteries of standardised assessment tools has enabled fairly good replication and comparison of findings. Comparing 19 non-alcoholic cirrhotics, with controls matched on age, sex and education, Moore et al.,

(1989) used the Benton Visual Retention Test, Trails A & B and reaction times to light, sound and choice stimuli. They found that 84% of the cirrhotic group failed two or more tests whereas none of the control subjects failed any tests. Generally, performance skills are impaired while verbal skills remain fairly intact (Moore et al., 1992). In particular, visuospatial, psychomotor and memory impairments have been reported in cirrhotics who are not overtly encephalopathic (Tarter et al., 1987a; Tarter et al., 1984; Hegedus et al., 1984; Giberstadt et al., 1980). The number connection test (Trails A, TMT A) has been reported to be particularly good at identifying LHE and its routine application has been recommended (Gammal & Jones, 1989). A number of studies have, however, found it to be one of the poorest indicators of impairment associated with LHE (O'Carroll et al., 1991; Moore et al., 1989). Many studies have found the digit symbol substitution and digit span subtests of the WAIS-R to be sensitive indicators of LHE (O'Carroll et al., 1991; Tarter et al., 1990a; Elsass et al., 1978; Schomerus et al., 1981; Gitlin et al., 1986; Dunk et al., 1988). Nevertheless, there is still no widespread agreement about which measures should be used, and it has been noted that many factors influence the nature and the extent of neuropsychological impairment in each person with liver disease (Tarter et al., 1988a). Some studies have attempted to evaluate treatment approaches to HE & LHE using neuropsychological test performance indicators (McClain et al., 1984; Egberts et al., 1985). Other studies have attempted to correlate neuropsychological test performance with biochemical measures associated with liver disease, therefore making early diagnosis of LHE easier. For example, Tarter et al. (1989) found that albumin and prothrombin time could explain a significant amount of the variance on neuropsychological testing in 79 non-alcoholic cirrhotics. They concluded that measures of functional liver status were related to cognitive capacity, even when impairment was not overtly evident.

1.3.2. Implications of LHE

The implications of the performance deficits found in LHE are significant and may lead to impairment of an individual's abilities to safely perform important activities of daily living, including driving (Schomerus et al, 1981; Rikkers et al, 1978; Gitlin et al, 1986). How much LHE impairs a patient's day-to-day functioning depends largely on the demands placed upon him or her (Schomerus et al, 1981). Further, under-diagnosis deprives patients with LHE of the opportunity to commence early treatment, and there is evidence that 50% of patients with LHE will develop HE within 6 months (Yen & Liaw, 1990).

1.3.3. The Role of Transplantation in the Investigation of LHE

Due to the reversible nature of LHE, it can be assumed that effective treatment of the underlying liver disease would eradicate the symptoms of LHE. The study of patients undergoing liver transplantation has provided a unique research paradigm in which the nature of the neuropsychological impairment can be studied, and initial results have been encouraging.

1.3.4. Neuropsychological Outcome of Orthotopic Liver Transplantation (OLT).

The work by Tarter and colleagues in Pittsburgh has produced some of the best controlled studies investigating the neuropsychological outcome of OLT. They assessed ten OLT recipients, approximately 3 years post-transplant, and compared them with 10 patients suffering from Crohn's disease (a chronic gastro-intestinal tract disease) on an extensive battery of tests (Tarter et al., 1984). No differences were found between the groups or when compared to population norms. The sample of OLT recipients was young (mean age 28 years) which may have influenced the positive results, and no pre-transplant data were included. In a larger, controlled

study, Tarter et al (1990a) evaluated 62 patients before, and an average of 60 weeks post liver transplantation, on a battery of neuropsychological tests. The battery was extensive and included the following tests: language capacity (token, animal naming, Shipley vocabulary); abstracting (Shipley abstracting); perception (Rey-Osterriech figure copy, trailmaking, block design, stroop); psychomotor (finger tapping, grooved pegboard, static ataxia); memory (digit span, digit supraspan, Benton visual retention, Brown-Peterson, dichotic numbers, Rey-Osterriech memory). They also included two control groups in the study; 22 patients suffering from Crohn's disease and 38 well matched healthy controls, all of whom were evaluated on two occasions. They found that prior to transplant, compared to healthy controls, liver disease patients were impaired on 12 out of 27 tests; those quantifying perceptual and visuospatial capacity and short-term memory. The performance of the Crohn's disease group lay somewhere between, and not significantly different to, that of the healthy controls and the liver disease groups. Upon repeat testing post-transplantation, only 4 out of the 27 tests discriminated between the transplanted and the healthy control groups. There was no differences between the Crohn's disease and the healthy control groups, and on only one test (digit symbol substitution test) were the transplanted group impaired compared to the Crohn's disease group. The authors noted that not all of the deficits displayed by the liver disease group prior to transplant were distinguishable from the Crohn's disease group, which suggested that a degree of neuropsychological impairment may accompany any chronic illness.

Similarly, Moore et al. (1992) assessed the cognitive function of 9 liver transplant recipients pre- and 30 days, 3 and 9 months post-transplant and compared them with 9 matched controls. They used a very lengthy assessment battery, the Wechsler Adult Intelligence Scale - Revised (WAIS-R), the Wechsler Memory Scale - Revised (WMS-R), The Rey-Osterreich figure and the Benton Controlled Aural Word Test. Liver

transplant recipients improved on tests measuring visual-motor co-ordination, perceptual organisation and attention. In contrast, the control group's performance did not change over time. No test data were included and no statistical analysis was reported, thus limiting the conclusions that can be drawn from this paper. A further study which failed to report any statistical analysis assessed neuropsychological status between 4 and 36 months post-operatively in 41 liver transplant recipients (Wolcott et al, 1989). This sample clearly comprises a very diverse group of patients, and no control group or pre-transplant data were available. Neuropsychological investigation included the following measures: controlled oral word association test; digit symbol substitution subtest (DSST) of WAIS-R; trailmaking tests A & B; Rey adult verbal learning test (RAVLT); number cancellation test; block design subtest of WAIS-R; and arithmetic subtest of WAIS-R. Respondents performed poorly on the DSST and the RAVLT. Interestingly, the authors reported that those subjects assessed greater than 12 months post-operatively performed worse than those assessed less than 12 months post-operatively.

Finally, a prospective study compared 11 OLT recipients with 9 heart transplant recipients using a battery of neuropsychological tests (Reither et al., 1992). Subjects were assessed pre-transplant, and at three monthly intervals up to one year post-transplant. Tests used were the mini-mental state examination (MMSE), California verbal learning test (CVLT), Wisconsin card sorting test (WCST), and the trailmaking tests A & B. Cognitive impairment was evidenced by the CVLT, the WCST and the TMT A prior to transplant in both groups of patients. Significant improvements over time post-transplant were noted for both groups in these tests. The MMSE failed to detect any cognitive impairment and it was concluded that it was not sensitive to the problems experienced by these patient groups. Collis et al. (1995) also used the MMSE with a group of liver transplant recipients and found that only one out of thirty patients showed impairment.

1.3.5. Conclusions: Neuropsychological Impairment Associated with LHE

In conclusion, the cognitive impairment associated with latent hepatic encephalopathy is now well documented by the use of neuropsychological tests, and several studies have investigated the neuropsychological outcome of liver transplantation. A wide variety of tests have been used, and a number have been recommended for specific use with this patient population. There is conflicting evidence concerning the efficacy of the Trailmaking A test, and due to the number of reports that it is insensitive to the impairments associated with LHE, its use with this population is not recommended. The digit symbol substitution subtest of the WAIS-R, however, has been reported to be a good indicator of neuropsychological dysfunction in this patient group. Further, the digit span subtest of the WAIS-R has also been recommended for use as a working memory test, although it also has a component measuring attention. The issue of improvements linked to repeat testing must also be highlighted, although it has been neglected by a number of researchers. Healthy control groups are essential to ensure that the effects of repeat testing can be excluded from the results reported. Further, the use of assessment tools which have parallel measures would be beneficial in studies with prospective designs.

1.4. The Role of Alcohol Abuse in Hepatic Encephalopathy

There is a large body of literature describing the neuropsychological disturbances demonstrated by alcoholics (e.g. Tarter et al., 1990b). Psychometric tests have identified memory, visuopractic, and psychomotor impairments in alcoholics (Wilkinson & Pavlos, 1987; Parsons & Farr, 1981). Considerable recovery of function with prolonged abstinence has been found, indicating that many of the cognitive deficits are not permanent (Grant, 1987; Brandt et al., 1983). There exists, however, considerable ambiguity regarding their aetiology. The neurotoxic effects of

ethanol are known, although it is now clear that many other factors, including psychiatric, genetic and medical factors, contribute to the neuropsychological deficits (Adams & Grant, 1984.). In particular, the effects of depression and poor liver function have been found to contribute to the cognitive problems experienced by alcoholics (Schafer et al., 1991). The neuropsychological deficits associated with depression have been well identified (Gilbert, 1984; Weingartner & Siberman, 1984), as have those associated with liver disease (see section 1.3.). Nevertheless, the deficits due to alcohol toxicity must be taken into account when investigating the neuropsychological outcome of liver disease and its treatment, including transplantation. In studies comparing alcoholics with and without cirrhosis, it has been shown that impaired liver function, probably as a consequence of HE, adversely affects neuropsychological capacity beyond that which can be accounted for by the effects of alcoholism alone (Giberstadt et al., 1980; Rikkers et al., 1978; Tarter et al., 1986a). Moore et al. (1989) used a battery of neuropsychological assessments on a group of 9 non-alcoholic cirrhotics (without overt signs of encephalopathy), a group of 10 alcoholic cirrhotics (without overt signs of encephalopathy) and two groups of healthy controls, matched to the alcoholic and non-alcoholic cirrhotics. They found no differences between the alcoholic and the non-alcoholic groups on any of the neuropsychological tests performed, but both performed significantly worse than the healthy controls (see Table 1). Thus the neuropsychological dysfunction detected in alcoholics with cirrhosis can be accounted for by LHE alone.

Table 1. Comparison of neuropsychological functioning of alcoholic cirrhotics with non-alcoholic cirrhotics, adapted from Moore et al. (1989).

Test	Alcoholic cirrhotics mean(sd)	Control group mean(sd)	Non-alc. cirrhotics mean(sd)	Control group mean(sd)
Benton VRT (correct)	5.5 (1.4)	7.6 (1.9)	4.0 (2.7)	7.7 (1.7)
Benton VRT (errors)	7.5 (3.6)	3.2 (2.2)	9.9 (6.0)	3.3 (2.6)
Trails A	37 (9)	32 (13)	52 (26)	39 (13)
Trails B	85 (32)	81 (22)	133 (91)	106 (44)
Reaction time-light	281 (76)	210 (31)	363 (179)	242 (34)
Reaction time-sound	316 (101)	241 (28)	423 (193)	231 (72)
Reaction time-choice	616 (216)	380 (116)	700 (146)	434 (78)

Similar results were reported by Rehnstrom et al. (1977), who found no difference in neuropsychological test results between a group of non-alcoholic cirrhotics and a group of alcoholic cirrhotics. Both these groups performed significantly worse than a group of alcoholics without cirrhosis, although no healthy control group was included for comparison. Finally, Arria et al. (1991) demonstrated improvement in cognitive functioning of 13 alcoholic cirrhotics one year following OLT, providing further evidence that a reversible HE underlies many of the neuropsychological deficits found in alcoholic cirrhotics pre-transplant.

In conclusion, the cognitive impairment experienced by alcoholic cirrhotics is both multifactorial and to a degree reversible upon abstinence and treatment for liver disease. Further, findings of similar cerebral

dysfunction in patients with cirrhosis, with different aetiologies, including alcohol, confirm the view that neuropsychological impairment in these groups is due to hepatic disease rather than alcohol. The inclusion of alcoholics in liver disease research is thus justified, and very common.

1.5. Psychological Adjustment to Chronic Illness

The impact that suffering from a life threatening disease has on the mental health of an individual can be vast. The literature on psychological aspects of physical disability provides a framework from which to understand the experiences of a patient suffering from chronic liver disease. There are a number of factors which may affect adjustment to a disability, including the age of onset, chronic versus acute onset, stability of condition and prognosis, severity of disability and degree of disability, intellectual functioning and personality change, and the presence of absence of pain (Wilkinson, 1995). There are three main theories about the psychological adjustment to disability: personality-based, social context and behavioural learning. The personality-based theorists liken disability to the experience of loss, in that the person will move through a series of stages or tasks in coming to terms with the disability. These stages include shock, denial, grief, anger and then finally adjustment. It is clear, however, that not all those who experience disability or illness go through these stages as a necessary step to adjustment. Further, there is no evidence of a relationship between severity of disease and psychological disturbance, which would be expected by a stage theory of adjustment. A second theory states that adjustment to disability is related to social networks and control over resources available, and therefore economic considerations are paramount (see Ben Sira, 1983 for review). Idealised images of normality, success and self-esteem being related to body-image and material well-being fuel prejudice against disabled people and have an impact on adjustment to disability. There is little evidence, however, to support this theory. The behavioural learning

theory of disability incorporates both of the above theories, stating that the adaptation to disability is a learning process, based on principles of classical and operant conditioning and the availability of rewards and reinforcements (Fordyce, 1971). The individual has to replace the loss of previously satisfying activities and goals, which depends both on the individual's abilities and the availability within the environment of alternative means of satisfaction. This theory certainly seems to provide a better understanding of psychological reactions to disability, in which the individual's behaviour and the environment within which the behaviour occurs are equally important.

Assessment tools used to measure the psychological reaction to disability and illness fall into three main categories, those specifically looking at the response to illness, those aiming to measure quality of life, and those measuring general measures of psychological distress. The present study aims to assess the psychological reaction to chronic liver disease and liver transplantation directly using the Acceptance of Illness Scale (AIS, Felton et al., 1984).

1.6. Psychological Reactions to Surgery

The literature on the psychological reactions to surgery is incomplete and confusing. Surgeons tend to neglect concerns about the psychological welfare of their patients when considering the need to reduce their waiting lists and boost their productivity figures. Nevertheless, the impact of good psychological adjustment to surgery can be great, increasing compliance and satisfaction, and resulting in faster recovery, thus placing fewer demands on the health service (Kincey & Saltmore, 1990). Positive responses to surgery can increase confidence, hope and self-esteem, whereas negative responses can lead to anxiety, depression and low self-esteem (Kincey, 1995). Surgical teams may find it difficult to assess a patient's subjective experience of surgery as the correlations between

subjective experience, overt behaviour and psychophysiology can be low (Kincey & Benjamin, 1984). Further, Miller (1987) has identified two types of coping responses to surgery, blunters and monitors. Monitors possess and seek more information about their health and treatment procedures, whereas blunters may be harmed by the presentation of 'unwanted' information. These difficulties mean that there is no simple way to predict the psychological outcome of surgery for an individual patient, and that the surgical team should be sensitive to the harm that can be done by routinely giving the same amount of information to every patient (Schultheis et al., 1987). Certainly, a degree of information giving is necessary in order to obtain informed consent for surgery, but much of the additional information available is optional.

1.6.1. Psychological Reactions to Surgery - Issues Facing an OLT Candidate

The assessment procedure for OLT is a lengthy process, during which the patient undergoes numerous investigations, from which the transplant team make the decision whether or not the patient is a suitable transplant candidate. If the patient is deemed a suitable candidate, it is ultimately the decision of the patient and his or her family whether or not to go ahead with the transplant process. This can be an agonising decision given that the patient often has to decide to have a transplant when he or she is fairly well, and may still have a life expectancy of a number of years, to give him or herself the best chance of surviving the transplant surgery. Further, the individual has to face the risk of death on the operating table.

1.6.2. Psychological Reactions to Surgery - Choice

Oncology literature provides tentative evidence that giving a patient a degree of choice of treatment options improves their psychological adjustment (Morris & Royle, 1988), although it must be noted again that individual differences must be taken into account, and an assessment of

the individual patient's coping style (blunter or monitor) is recommended. Further, there is the risk that giving the patient a degree of responsibility for the treatment decision could lead to them assuming responsibility for treatment outcome. This becomes a problem if post-operative complications develop. Discussions about the risks involved in the procedure are therefore fraught with psychological complexity. Ideal practice involves providing opportunities for patients to gain information and advice if they wish. There is some evidence that greater long-term psychological disturbance occurs with major rather than minor surgery, for example with oncological surgery (Maguire, 1985), and cardiovascular surgery (Mumford et al., 1982).

1.6.3. Psychological Reactions to Surgery - Conclusions

It is clear that the factors affecting psychological outcome of surgery are complex, including both patient characteristics and particular dimensions of the surgery planned. Such dimensions include the extent to which surgery may restore or remove function, change in life expectancy, change in incidence of pain, change in the level of self-care, and the degree of visible mutilation. In the case of liver transplantation, both positive and negative outcomes along these dimensions may occur, complicating the picture further. Symptom substitution may occur post-operatively, in that the symptoms of chronic liver disease may be replaced with new symptoms such as the side effects of immunosuppressant medication, complications of the surgery or recurrent infections.

1.7. Quality of Life

Quality of life (QoL) is one of the most poorly defined and confusing concepts in modern medicine (WHOQOL group, 1995). Some of the early discussions of QoL saw it very much as a function of material well-being, in other words how much money a person had (WHOQOL group, 1995;

e.g. Harland, 1972). Since then the emphasis has shifted to include objective measures, such as age, sex, education level, work status, and subjective measures, that is the individual's perceived sense of well-being in a number of domains. The first major studies equating QoL in these terms, usually focusing on objective or subjective measures, attempted to measure the QoL of samples of the general public (e.g. Krupinski, 1980; Campbell, 1981). More recently, health-related QoL, in particular the impact illness has on a person's functional status and happiness (Bergner, 1985), has been the focus of study. Interest in this field started with work with cancer patients and the bulk of the literature continues to be with this patient group. For a long time in health-care settings the primary aim of medical intervention was increasing the duration of a person's life. Morbidity (illness) and mortality were the only outcome measures used to evaluate the effectiveness of a treatment (Bergner, 1989). The focus of QoL work with cancer patients , however, has highlighted that living longer was not necessarily the most important thing to the patient, and in fact their QoL was often more important (Hunt et al., 1991; Morrow et al., 1992). As a result of this work it has been slowly recognised in many fields of medicine that goals of health care should be twofold: to increase the duration of a patients life and to improve their QoL. Indeed, forty years earlier the World Health Organisation seemed well ahead of its time when it defined health as a state of physical, social and mental well-being, not merely the absence of illness (WHO, 1958). Although this recognition has been a major development in the philosophy of health care, the large body of QoL literature to support the importance of evaluating treatments in terms of QoL is generally fundamentally flawed. Most researchers working on QoL, in whatever field, use their own, usually implicit, definition of QoL. The subjective nature of QoL tends to elude strict definition and makes a universal definition very difficult. Further, the poor use of well validated and reliable measures of QoL makes comparison of different studies difficult, and replication virtually impossible. In addition, health-related QoL is not a steady state, but

changes constantly with the adaptational process over the course of a chronic illness and its treatment. Generally, in most studies at present, QoL can be defined most typically to encompass physical, psychological and social functioning (Aaronson et al., 1991).

1.7.1. Quality of Life Associated with OLT - Methodological Issues

The methodological difficulties described above are very apparent in the emerging studies of QoL of orthotopic liver transplant (OLT) recipients. As in other fields of medicine, over the past ten years there has been a small surge of interest within liver transplant units to evaluate this major surgery in terms of the recipients' QoL post-transplant. OLT is seen as the treatment of choice for end-stage liver disease. Individuals suffering from chronic liver disease may have led restricted lifestyles for a number of years because of physical difficulties including pain, fatigue, chronic itching, and neuropsychological difficulties due to hepatic encephalopathy (described section 1.3.). Further, social difficulties and secondary mood disturbance due to stress may be expected. Although very few studies assessing QoL post-transplant have used the same measures, universally positive results have been reported. A number of these studies, and relevant issues as they arise, will now be discussed.

1.7.2. Quality of Life Associated with OLT - Studies that use Objective Measures

Using the purely objective measures of return to work and need for medical care, Lundgren et al. (1994) retrospectively investigated 197 transplant recipients. They reported that 64% had returned to work between 6 and 12 months post transplant and only 1% still needed care in an intensive care unit, compared to 17% and 23% respectively before they received their transplant. The mean age of the sample was 36 years. The authors concluded that OLT enhanced the recipients' capacity to work and

diminished their need of medical care, thus improving their QoL. Similarly, the QoL of 46 transplant recipients (including 15 infants, 13 adolescents and 16 adults) was assessed one year post-transplant by their return to work or school (Starzl et al., 1979). The authors reported that QoL of their sample ranged from poor to good. The methodological difficulties of this study include no pre-transplant data, no control group and the grouping of diverse age groups together. Another retrospective study of 126 OLT recipients (mean age 44 years) assessed QoL, investigating a new type of immunosuppressant medication, by the patients' ability to work, and ability to take part in social activities, using a standardised questions over the telephone (Felser et al., 1991). Positive results in both domains were reported , and the authors concluded that the change in medication had improved the QoL of the recipients interviewed. No control group was included and no measures were taken before the change in medication. In all of the above studies the use of objective indicators assumes that they are valid indicators of QoL (Najman & Levine, 1981). The evidence in the literature is that the relationship between objective criteria for QoL and how an individual perceives his or her QoL is very complex and therefore relying on objective criteria to make assumptions about an individual's QoL is insufficient (WHOQOL group, 1994). The above studies highlight the difficulties inherent in reviewing the field of QoL research. The term QoL is used liberally without a clear understanding of its multidimensional nature, and consequently the danger is that over-enthusiastic conclusions can be reported about the outcome of treatments.

1.7.3. Quality of Life Associated with OLT - Studies that Combine Objective and Subjective Measures

Other studies combine objective and subjective measures, but still base strong conclusions about the QoL of OLT recipients on the objective measures, particularly returning to work. In a retrospective study with 46

OLT recipients, mean age 46 years, Eid et al. (1989) assessed QoL in terms of the patients' subjective sense of well-being (from simple questioning) and their employment status. The recipients were interviewed between 13 and 31 months post transplant. Subjective well-being and satisfaction with life were reported by 91% of recipients. Of the 46 recipients, 26 were employed, 16 were homemakers and 4 did not work. There are a number of criticisms that can be made about this study. Firstly, no pre-transplant data were collected, and no control groups were included. Further, the simple subjective rating of well-being and satisfaction with life combined with employment status are insufficient components of QoL.

1.7.4. Quality of Life Associated with OLT - Studies that have used Questionnaires Compiled by the Authors

Another group of studies have attempted to assess QoL in terms of the patients' ratings of a number of dimensions, but have failed to use standardised measures, which prevents replication and comparison of results. In 26 OLT recipients (greater than 6 months post-transplant, mean age withheld), QoL was assessed using likert-type scales on what is described as a questionnaire compiled by the authors for the purpose of the study (Foley et al., 1989). The authors reported that the sample experienced a low number of side-effects of immunosuppressant medication and 91% rated their QoL as good, very good or excellent. Again, no pre-transplant data or control groups were included. Nicholas et al. (1994) assessed QoL after OLT in 166 recipients (mean age 45 years) at least one year post-operatively. The authors developed a five-part questionnaire, the Rehabilitation Medicine QoL Instrument, to measure the QoL of the sample. This included items about physical functioning, endurance, vocational role and financial status. A high level of musculoskeletal weakness was noted among the sample, although they were able to perform activities of daily living well. Fewer recipients were working than had been before their transplant, and this was linked to the

musculoskeletal problems, marital status (more likely to be working if married) and longer duration of liver disease. The same criticisms of no control group and no pre-transplant data (employment status was assessed retrospectively) apply to this study.

In a recent longitudinal, multicentre study, 346 adult transplant recipients (median age 48) were assessed before and one year after OLT (Belle et al. 1997). The authors compiled their own QoL assessment battery by taking particular items from a number of standardised instruments. They assessed five domains: disease; psychological distress and well-being; personal function; social/role function; and general health perception. They reported improvements in all domains post-transplant, and concluded that *"... liver transplantation markedly improves the quality of life of patients with end-stage liver disease."*. The most common distresses reported by the patients both before and after surgery were fatigue and muscle weakness. Psychological distress was noted by 57% to 64% of recipients, although it was more likely to have decreased than increased post-transplantation. The longitudinal design of this study certainly aids interpretation of the results, although this is limited by the lack of a control group. Further, the process of compiling a new questionnaire from items from existing scales is a practice to be criticised as no reliability of validity data have been established. The authors did, however, supply the complete questionnaire in the appendix, which will allow replication. Similarly, Levy et al. (1995) used a questionnaire, the National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases liver transplantation QoL form (NIDDK QoL) in a prospective study involving a total of 573 transplant recipients, at pre, 1,2 and 5 years post-transplant. This was derived from items from a number of standardised instruments: Karnofsky Performance Status Scale; Sickness Impact Profile; Index of Well-Being; Medical Outcomes Survey; and the Nottingham Health Profile. The authors noted that each of the above instruments were designed to be administered by the interviewer, although the NIDDK

QoL was self administered. Further, and of importance to the validity of the data, no restrictions were placed or friends of family helping the patients to fill out the form. Another significant limitation of this study was the cross-sectional design, in that the same subjects were not serially assessed. Rather, different groups of subjects at each time points were assessed. Finally, no control group was included in the study. The NIDDK QoL contained five sections: patient demographics; occupation; symptom distress/frequency; activities of daily living; and impact of health on daily life. Improvements in all domains were noted at each post-transplant time point, particularly in perception of health status, self-image and ability to function. The authors concluded that OLT leads to improved QoL by one year post-transplant and this improvement is sustained by five years post-transplant and beyond.

Comparing QoL in 10 individuals after liver transplantation for cancer with 68 patients transplanted due to non-malignant diseases, Boudet et al. (1995) used a number of indicators of QoL: side-effects of medication; constraints of medical follow-up; and a self-report rating item from the Sickness Impact Profile (see section 1.7.5.). They concluded that in terms of the quality of life rating, there was no difference between the two groups between 1 and 24 months post-transplant. 76% of the total sample rated their QoL as normal. The authors noted that this was lower than figures reported in previous studies, but within normal population ranges. The measures used in this study were inadequate to equate QoL and no pre-transplant scores or control groups were included.

1.7.5. Quality of Life Associated with OLT - Studies that have used Standardised Measures

The final group of studies that will be discussed are those in which complete standardised instruments have been used. The two most commonly used instruments are the Sickness Impact Profile (SIP) and the

Nottingham Health Profile (NHP). The SIP is a generic health status instrument developed in the United States, measuring the impact of disease on a patient's life. It includes a physical dimension, a psychosocial dimension and a number of other categories: sleep and rest; eating; work; home management; and recreation and pastimes. Its reliability and validity are good (Bergner, 1993). The NHP is another generic health status measure and consists of two parts. Part 1 includes energy, pain, emotional reactions, sleep, social isolation and physical mobility. Part 2 includes employment status, jobs around the house, social life, family relations, sex life, hobbies/interests and holidays. Validity and reliability have been established (McEwan, 1993). The NHP has, however, been criticised for focusing on problems and failing to reflect any positive aspects (Bergner, 1985).

One of the most prolific research teams investigating the QoL of liver transplant recipients is based at the University of Pittsburgh. A cross-sectional design assessed QoL in 10 patients greater than 3 years post-transplant (mean age 28 years) using the SIP (Tarter et al. 1984). A control group of 10 individuals suffering from Crohn's disease (mean age 39 years) was included, although no healthy control group was included. No differences between the two groups were found, and impairments in sleep and rest, eating and appetite, work capacity, and recreation and pastimes were noted in the transplant group compared to population norms. Omission of pre-transplant data limits the interpretation of these results. A number of years later, Tarter et al. (1991) investigated QoL in 53 OLT recipients prior to and again approximately 3 years post-operatively. The SIP and the Social Behaviour Adjustment Schedule (SBAS, administered to an informant of the patient) were used. A healthy control group, N=35, was included although they only completed the SIP on one occasion. Significant improvements across all dimensions and categories were reported post-transplant, although some impairments did persist with respect to social interaction, home management, recreations and pastimes,

sleep and rest. Further significant improvements were reported on scales of disturbed behaviour, social role performance and burden on the SBAS, and at the post-transplant stage there were no differences in scores between OLT recipients and healthy controls. The authors concluded that OLT significantly improved QoL, although not to the level of functioning of healthy individuals. Further, they concluded that at three years post-transplant greater improvement was apparent in physical rather than in psychological processes. The following year the same group again reported improvements across almost all of the dimensions of the SIP greater than 2 years post-transplant, compared to pre-transplant scores (Tarter et al., 1992). No control group was included in this study. Riether et al. (1992) compared the QoL outcome of 61 liver transplantation recipients with that of 51 heart transplant recipients using a battery of measures assessing psychiatric status, cognitive functioning and QoL. QoL was assessed by the SIP. The mean age of both groups was 46 years. The subjects were assessed prior to their transplants and at three month intervals up to one year post-transplant. Significant improvements on the physical, the psychosocial and the overall scores of the SIP were recorded by both patient groups post-operatively. This study provides replicable evidence of improved QoL post OLT, although it can be criticised for failing to include a healthy control group and its conclusions must be limited to the first year post-operatively. After the first year change in the QoL of recipients may begin to appear.

1.7.6. Quality of Life Associated with OLT - 'Faking Good'

'Postoperative euphoria' of transplant recipients has been described by a number of workers (e.g. Leyendecker et al., 1993). Recipients have described the feeling of being 'reborn' after surviving a transplant procedure, particularly when they have been chronically ill for many years and a transplant was their last chance of survival. Further, patients report feeling indebted to the organ donor, their family for the support they have

given, and to the transplant team. This point is important in the field of QoL research, where it is highly possible that recipients feel pressured into reporting that they feel great. They may feel guilty if they admit to the medical team who saved their lives that they are having problems. This is particularly important given the publicity given to the high cost of transplant procedures. Finally, it may be that transplant recipients exhibit a degree of denial and find it hard to communicate their fears about organ rejection. It is likely that more useful information about the QoL outcome of transplantation would be gained at a later postoperative stage, when the recipients may feel more able to be truthful about any difficulties that they are experiencing.

1.7.7. Quality of Life Associated with OLT - Problems with Measurement

The NHP was used to assess QoL in 58 OLT recipients (mean age 42) in a cross-sectional design including three time points: less than a year, 1-2 years and more than 2 years (Lowe et al., 1990). Overall the results indicated that QoL was high in OLT recipients, equivalent to age and sex matched general population norms (no control groups were included in the study). The authors acknowledged that the NHP is weighted to negative aspects of health, and highlighted that many of the recipients indicated that it gave the no opportunity to comment on the positive aspects of their experiences. It can therefore be concluded that the NHP is an insufficient measure to assess QoL in this patient group, masking positive aspects and perhaps also insensitive to subtle changes in QoL experienced. Further, the results would carry more weight if a prospective design had been used. A further study reporting results from the NHP assessed 27 OLT recipients, 71 patients with chronic liver disease assessed for transplant but not yet transplanted and 11 rejected for transplantation (Price et al., 1995). They were prospectively assessed at 3-6, 9-12, and 15-24 months post-transplant. Results indicated that over 2 years post-transplant QoL, as assessed by the NHP, improved and became broadly

similar to that of the general population (no healthy control group was included). Over the same period, very little change was observed for the non-transplant group. The authors highlighted that the two groups differed in the diagnostic mix, severity of liver disease and their QoL at the beginning of the study, and therefore it cannot be assumed that the QoL of patients in the non-transplant group would have improved had they undergone transplantation. Transplant recipients, despite rating their overall health as good, did experience a number of problems with pain, mobility and looking after the home. No statistical analyses of the data were presented and no pre-transplant data were available. It was concluded that OLT improved QoL but not to optimal levels.

A Dutch group investigated QoL in 46 adult OLT recipients, some of whom were assessed serially, pre- and yearly post-transplant, and some assessed at one time point only (Bonsel et al., 1992). The researchers combined the data from both groups in a cross-sectional analysis. A computer assisted battery of assessments were used to examine QoL and psychiatric status. QoL was measured by the NHP, the Karnofsky index which is a global one-item measurement of health status (not designed as a QoL measure although often used as one), and the Index of Well-being which is a global measure of experienced well-being. Further, they asked specific questions about the following areas: activities of daily life; physical complaints; and satisfaction with health, leisure time, daily activities and life as a whole. The authors noted that pre-transplant scores suggested restrictions in all domains of life, especially low energy levels. There were improved scores in all the assessments used post-operatively, although not to the level of general population norms. Due to the relatively small sample size given that different patients were assessed at each time point, and the lack of any control groups, interpretation of this data must be made with extreme caution. This study also highlights another difficulty when evaluating QoL research, namely that the use of QoL measures translated for use in different languages is a practice open to criticism.

Fletcher et al. (1992, pp. 1145-1146) described the problems as follows: *"Researchers should be wary of using an instrument in a cultural setting different from that in which it was developed. Apart from face or content validity, other problems include the validity of the translations and the relative importance of items in the instrument."* Another study which used translated measures investigated the following: physical and psychological status; physical complaints; capability to participate in daily life; social support; and global QoL in 45 OLT recipients an average of 9 months post-transplant (Leyendecker et al., 1993). A German translation of the Psychological General Well-Being Index, including a number of adaptations, was used and global QoL was measured by means of a visual analogue scale. Assessments of mood and social support are discussed elsewhere (see sections 1.8. and 1.10. respectively). Results indicated that QoL in the first year post-transplant was good: 60% high, 31% medium and 9% very bad. Those who were actively working again reported feeling best. Positive subjectively reported QoL occurred despite a high number of physical complaints. Thus the authors concluded that an improved QoL is not implied merely by absence of complaints. As with most studies described above, no pre-transplant data and the lack of a control group limit the interpretation of these results.

Chen & Sun (1994) take the view that simple and concise measurement of QoL is preferable to the use of complicated instruments, indicating that in their view standardised instruments are unnecessary. Unfortunately, although standardised instruments may be complicated, it is only through their use that we can compare findings across groups, and that conclusions about the QoL of transplant recipients can be made with confidence. They used the Karnofsky index and the Zubrod-ECOG-WHO as well as a number of medical objective measures, such as liver and renal function, and number of postoperative infections to assess QoL in 7 young OLT recipients (mean age 20 years). The mean time since transplant was 40 months (ranging from 2-8 years). The authors did not carry out any

statistical analysis of results, but concluded that the majority of patients showed a high degree of satisfaction and enjoyed an "excellent" QoL with complete rehabilitation after OLT. These are clearly over-enthusiastic claims given the methodological flaws of the study. The sample size was very small (N=7, including one pre-school child) and no control groups were included. Further, the time since transplant varied considerably and no pre-transplant data were included. Finally, the assessment measures were insufficient indicators of QoL.

1.7.8. Quality of Life - Development of New Measures

A disease specific QoL measure, the European Organisation for Research of Treatment of Cancer (EORTC), was modified for use with a liver disease population by Kuchler et al. (1991) who presented results from 12 OLT recipients. This measure includes items on: functional status; ability to work; general symptoms; symptoms specific for liver disease; anxiety; depression; social integration; treatment strain; overall physical condition; and overall quality of life. Unfortunately demographic data on subjects were incomplete. Further, a healthy control group and a chronic liver disease control group were assessed on one occasion but again no data were included. Data were collected from two transplant centres; Chicago and Hamburg. Patients from the former centre were assessed at 3, 6, 12, 24 and 36 months after OLT (N=38). Patients from Hamburg were assessed pre- and 2, 6, 12, 24 and 36 months after transplantation (N=9). Results indicated that successfully transplanted subjects perceived their overall QoL as significantly improved after transplantation, as high as the healthy controls and better than the chronic liver disease patients. Perception of their overall physical condition also improved post-transplant although not to the levels of the healthy controls. The interpretation of results from this study is limited by the poor reporting of demographic data of the patients and controls. Further, the combination of results from two

centres must be undertaken cautiously given the different languages involved and the timing of assessments.

A number of health and psychosocial measures were used to investigate QoL in 41 OLT (mean age 44 years) recipients between 4 and 36 months post-transplant (Wolcott et al., 1989). The Index of Well-Being and the Simmons Scale of self-esteem were combined with a number of direct questions about: current life satisfaction; illness-related stressors; vocational activity; social/leisure activities; social support; global health; activity restrictions; physical symptoms; and recent use of health services. Neuropsychological assessments were also used and were discussed elsewhere (see section 1.3.4.). Positive life satisfaction was reported in all domains except work, career and sexual activity. High self-esteem was also reported, and the most stressful areas were reported to be related to financial matters and medical treatment. Finally, 75% rated their health as good or better, although 80% and 48% had some restriction in rigorous activity and moderate activity respectively. The main criticism of this study (aside from lack of control groups and no pre-transplant data) was the wide range of transplant to assessment intervals included in the sample. Additionally, no statistical analysis was reported on the data.

1.7.9. Quality of Life - Summary of Issues Associated with OLT Research

In conclusion, there have been a number of studies assessing QoL associated with liver transplantation recipients. Many of them, however, are methodologically flawed: they are often retrospective; lack control groups; use unreliable and invalid measures of QoL; and employ small sample sizes. Perhaps the most important criticism is the practice of making unrealistic conclusions about the QoL of OLT recipients, given the above flaws. Heterogeneous groups of subjects, for example with vastly varying times since they received their transplant, is also a criticism of many studies. The better studies have acknowledged that an improvement in QoL does occur post-transplant, although not to levels

observed in the general population. Finally, the problem of recipients reporting a better QoL due to gratitude to the transplant team must be acknowledged.

1.8. Psychological Dysfunction Associated with Liver Transplantation

As well as the neuropsychological difficulties concurrent with HE, the emotional accompaniments of liver disease are assuming greater importance given the improved prognosis provided by OLT. Studies assessing the emotional well-being of those suffering from liver disease have focused on anxiety and depression in transplant recipients. Some of these studies are prospective and therefore include pre-transplant data, giving an indication of the mood state of those suffering from chronic liver disease. Generally, however, the assessment of mood in OLT populations is limited.

1.8.1. Psychological Dysfunction in Oncological Populations

In contrast, there is a large body of literature documenting high levels of anxiety and depression in oncological patients (Peck & Bolond, 1977; Forester et al., 1978; Greer, 1984; Palmer et al., 1980). Most of these studies concluded that anxiety and depression were associated with the treatments the patients were undergoing (chemotherapy and radiotherapy). Other researchers have found emotional distress in cancer patients to be more related to situational factors, such as home support and other stresses, rather than illness (e.g. Weisman, 1976). Hinton (1984) found that the longer the illness the greater degree of emotional disturbance to be expected. Maguire (1984) has highlighted the under-diagnosis of psychological disturbance in cancer patients, and suggested the use of specially trained doctors or nurses to help to identify those at risk, as well

as those already suffering from psychological disturbance, in those who are seriously ill.

1.8.2. Problems in Assessing Psychological Disturbance in Physically Ill Populations

One major problem in assessing psychological disturbance in physically ill populations is that many of the items used to indicate morbidity in the general population occur as accompaniments to serious illness, such as fatigue, loss of appetite and sleep disturbance. The Hospital Anxiety and Depression Scale (HADS) was developed specifically for use with medical patients, excluding somatic features (Zigmund & Snaith, 1983). It is extremely easy to score and administer, and is extensively used in many settings, providing evidence of good validity and reliability.
Unfortunately, most of the studies assessing psychological disturbance in the liver disease population have used scales measuring mood that still include somatic items, weighting them towards those who are physically ill. Therefore results must be interpreted with caution, as there is a risk of over-reporting of psychological disturbance.

1.8.3. Studies Assessing Psychological Disturbance in OLT Populations

The Beck Depression Inventory (BDI) and the State Trait Anxiety Inventory (STAI) were used to assess emotional status in 9 heart and 11 liver transplant recipients pre- and at 3 month intervals up to 1 year post-transplant (Riether et al. 1992). The authors noted significant improvements in depressive symptoms after transplantation in both groups. Mild to moderate anxiety was also present in both groups, which dropped considerably at 3 months before rising again at 6 and 12 months post-operatively. The STAI and the Zung Self-rating Depression Scale were used to assess emotional status in 52 OLT recipients, 26 whom were tested at one time point post-operatively and 26 whom were assessed

prospectively pre- and 3 months post-transplant (Bonsel et al., 1992). Three months post-operatively there was a significant improvement in depression scores, although no control group was included for comparison. No change in reported anxiety was found. Using open-ended psychiatric interviews, House et al. (1983) assessed the psychiatric status of 20 adult OLT recipients pre- and post-operatively (ranging from 6 months to 12 months since transplantation). According to DSM III criteria, they found that pre-transplant 95% of patients experienced significant psychiatric distress, which rose to 100% post-operatively. The most common problems were organic brain syndromes, anxiety and depression. In contrast, the authors reported that using the same criteria, 17% pre- and 32% postoperative kidney transplant recipients experienced significant psychiatric distress. There were no control groups included in this study and the times since transplant varied considerably, therefore masking any changes in psychiatric morbidity in this group over time. Finally, the open-ended questioning technique is open to criticism given that no validity or reliability was established, and replication of the study is not possible. The use of standardised assessment measures must be recommended.

The Profile of Mood States (POMS) has also been used. Wolcott et al. (1989) used the POMS with 41 OLT recipients, between 4 and 36 months post-transplant, and reported minimal mood disturbance in this group. No pre-transplant data or control group were included. In a prospective, controlled study, Moore et al. (1992) assessed 9 OLT recipients, and 9 well matched controls at the same intervals, pre-transplant and 30 days, 3 and 9 months post-operatively. A decrease in tension, depression, confusion, anger and fatigue, and an increase in vigour were found in the OLT group post-operatively. There were no changes found in the control group.

Psychological dysfunction has also been reported in other studies as a component of quality of life scales. Using the EORTC QoL questionnaire,

which has components of anxiety and depression included, Kuchler et al. (1991) assessed 12 patients pre- and 3, 6, 12, 24 and 36 months post-operatively (although not all patients were assessed at every time point). Healthy controls were also assessed at one time point, but no data were included to indicate how well matched they were. They found that transplant patients experienced higher anxiety than the control group, and that it stayed high post-operatively, even at three years. They also noted that reported anxiety increased immediately in any crisis situation, for example in situations of infection or rejection. Depression, on the other hand decreased with time post-transplant. The authors also reported a sex difference in that women reported less depression, which is in contrast with elevated levels of depression in women compared to men in the general population. The small sample size and lack of statistical analysis limit the usefulness of the results presented in this study, although it highlighted a number of interesting points that require further investigation.

Finally, Tarter et al. (1984) reported on the mood components of the Minnesota Multiphasic Personality Inventory (MMPI) and the Sixteen Personality Factors Questionnaire (16PF) in 10 OLT recipients (3 years post-transplant) and 10 controls suffering from Crohn's disease. No differences were reported between the two groups, although compared to population norms, the OLT group displayed higher anxiety, somatic distress, depression, worry and social withdrawal. The transplant recipients in this study were relatively young, with a mean age of 28 years, and no information is available about the change in mood over time.

1.9. Self-Esteem

Self-esteem can be defined as the perception an individual possesses of his or her own worth (Hattie, 1992; Rosenberg, 1989). Elements of self-esteem include genetic influences combined with the impact of life experiences

(Battle, 1990). Generally, however, self-esteem is a fairly undefined concept, often confused with the wider domain of self-concept, or the more specific self-perception of body image (Brinthaupt & Erwin, 1992). In the field of health psychology, self-esteem has been described as a mediating resource in the psychological adjustment to illness (Rosenberg, 1989). There has, however, been little research into the role of self-esteem in populations with life-threatening illnesses, and very little in the field of psychological outcome to liver transplantation. The present study aims to assess the self-esteem of OLT recipients to establish if it is equivalent to that of healthy subjects. Wolcott et al. (1989) used the Simmons scale of self-esteem with a group of 41 liver transplant recipients between 4 and 36 months post-transplant, and reported levels of high self-esteem. Given that the definition of self-esteem is the individuals' perception of their own worth, the return of healthy functioning post-transplantation and the sense of a "new life" may predict that OLT recipients would have a higher self-esteem than liver disease controls. The relationship between low, or high, self-esteem and health is unknown.

1.10. Social Support

The concept of social support in relation to coping with health problems is complex. A number of studies have found that a positive appraisal of social support has been related to positive emotional adjustment to illness, as well as important health-related outcomes, including mortality (Namir et al., 1989; Vanderplate et al., 1988). As in many fields of health psychology research, the bulk of the literature focuses on oncology populations, but much of the work can be generalised to other life-threatening illnesses. It is now well recognised that various forms of social support exist for an individual. A good distinction, particularly relevant to chronically ill populations, is that of emotional and practical support (Power et al., 1988). These authors have also distinguished between actual and ideal levels of social support, and the importance of

any discrepancy between these. This approach to social support allows the adequacy of social support functions to be analysed, rather than just the number, type and organisation of an individual's support system. It has been postulated that the type of support needed by an individual changes over time, and as stages of illness progress (Britton et al., 1993). Therefore the adequacy of support will depend on the extent to which changing needs are met by significant others. Indeed there is good evidence that an individual can influence the nature of the social support they receive (Dunkel-Schetter et al., 1987). In work with cancer patients, this group found that the adoption of a positive attitude was a conscious effort to elicit support from others (Dunkel-Schetter & Wortman, 1982). The nature of the relationship between social support and health may be bidirectional. That is, good social support may lead to better health outcomes, and vice versa (Gotlib & Hooley, 1988). The cancer literature sheds further light on the relationship between social support and health with evidence that one of the worst stresses reported by patients is the breakdown of social contacts, during a time when the need for support is heightened (Gore, 1981). Two effects of social support have been described, direct and indirect (Cohen & Wills, 1985). Direct effects reduce stress responses of the individual by changing their perceptions and cognitions of the threat they face, or by changing physiological processes at a result of decreased tension or increased relaxation. Indirect effects of social support include bringing about changes in the individual's health-related behaviour, for example by reducing alcohol consumption. The role of social support in adjustment to liver transplantation has received little attention. The importance of social support in this group of patients must be understood in the context of the impact of a debilitating chronic illness, with associated role losses due to fatigue and other symptoms. The need for practical support may be great. In contrast, the transplant process may necessitate a greater need for emotional support. Post-transplant, the need for support may be complex, with the individual hoping to regain much of the practical and emotional independence they had prior to their

illness. Added to this, coping responses such as denial (see section 1.7.6.) may mask their true need for support. This study aims to assess transplant recipients' perceptions of the quality of their social support, and to assess the relationship between inadequate (too much or too little) social support and QoL.

1.11. Overall Conclusions

The neuropsychological impairment associated with latent hepatic encephalopathy is now well documented. A number of studies have shown that performance on neuropsychological tests improves post-transplant. The quality of life of transplant recipients has received a great deal of interest in the literature, although due to its poorly defined nature, and methodological flaws in many studies, conclusions must be drawn with caution. QoL does seem to improve after a liver transplant, although not to the levels found in the healthy population. Very few studies have looked directly at changes in anxiety and depression post-transplant, and those that have tended to use scales that are inappropriate for use with physically ill populations. The time since transplant has been ignored by many studies, with the inclusion of patients at vastly different times since transplant. The majority of studies have included patients within the first year post-transplant. It may be that the above variables change at different rates, and it must be acknowledged that changes found may be limited to certain phases post-transplant.

It is clear that there is a need for well controlled, prospective research into the psychological outcome of liver transplantation. OLT is a procedure which involves great risk to the patient, not only in terms of dying on the operating table with a life expectancy of a number of years, but also of months of risk of infection or rejection. A lifetime of strict drug regimens is also a major adjustment. Nevertheless, successful OLT can dramatically restore an individual's health, and their associated roles and activities.

For most people, psychological issues are paramount, and can often be overlooked by those around them. It is essential that QoL, mood and neuropsychological function are adequately assessed in these individuals, and that their psychological needs are met. The importance of establishing mediating factors to psychological adjustment to liver transplantation is a further research challenge.

1.12. Aim of the Present Study

The major aim of the present study is to investigate the psychological and cognitive sequelae of liver transplantation. A prospective design was used to assess OLT recipients pre- and 3 years post-transplantation. A liver disease control group, who have not undergone OLT, and two healthy control groups have been included. The following hypotheses were tested:

1.13. Hypotheses

1. Liver transplant recipients will have improved on mood (anxiety and depression), quality of life and neuropsychological measures.

2. The liver disease control group will have deteriorated on mood, quality of life and neuropsychological measures.

3. The healthy control group will show no change on mood, quality of life and neuropsychological measures.

4. Self-esteem of liver transplant recipients will match that of healthy controls, whereas liver disease controls will have lowered self-esteem.

5. Transplant recipients will have a more positive acceptance of illness than chronically ill liver disease controls.

6. Inadequate perceived social support will be associated with poorer QoL and higher levels of anxiety and depression.

CHAPTER 2. METHODS

2.1. DESIGN

A repeated measures experimental design looking for both within group differences, and between group differences, on a number of measures was used to assess the long-term psychological and cognitive impact of liver transplantation. Subjects were assessed at two time points, between 3 and 5 years apart. Four groups were included in the study: liver transplant recipients (Tr), chronic liver disease controls (LC) and two healthy control groups, one included in both repeated and cross-sectional analysis (HC 1), and a better matched group included in the cross-sectional analysis only (HC2).

2.2. SUBJECTS

A total of 78 patients with liver disease attending the Royal Infirmary of Edinburgh for treatment underwent the initial assessment for the study (Time 1) between 1993 and 1994. Of this group, 28 subsequently underwent liver transplantation. The mean time between transplantation and follow-up assessment was 37.4 months (sd=10.5). At the follow-up stage (Time 2), confirmation of whether each person was alive or dead was obtained, and it was found that 7 of the transplanted group and 28 of the non-transplanted group had died since the initial recruitment for the study. A Chi squared test indicated that the difference in mortality rates between the two groups (Tr and LC) was significant ($x=6.97$, $p<0.01$). The remaining patients, 21 liver transplant recipients and 22 chronic liver disease controls, were contacted by post asking them whether they would take part in the follow-up assessment (see Appendix 1 for letter). Self-administered questionnaires (see Chapter 2), a consent form (see Appendix 2) and a postage paid reply envelope were included. Positive replies were received from 16 liver transplant recipients and 11 non-transplanted

patients. One transplant recipient did not wish to take part in the study. Appointments were then arranged to meet with those who agreed to take part in the study to carry out the neuropsychological assessment. At this point one of the non-transplanted patients had died since completing the self-administered questionnaires, one transplant recipient lived in Northern Ireland and it was therefore impossible to arrange a meeting, and one transplant recipient and one non-transplanted could not be contacted. The final samples therefore included 16 liver transplant recipients (14 of whom completed the neuropsychological assessment) and 11 non-transplanted controls (9 of whom completed the neuropsychological assessment). All patients had biopsy confirmed liver disease at the initial assessment stage.

Table 2: Liver disease characteristics of transplanted and non-transplanted groups.

Liver disease characteristic		Transplant group	Liver disease control group	X	p
Child's score	A	0	1	0.49	NS
	B	9	7		
	C	7	3		
Type of liver disease	Alcoholic	4	4	0.40	NS
	Primary biliary cirrhosis	6	4		
	Primary sclerosing cirrhosis	2	1		
	Cryptogenic cirrhosis	2	0		
	Chronic active hepatitis	2	2		

Chi squared tests were carried out to determine whether the transplant group (Tr) and the liver disease control group (LC) were matched in terms of liver disease characteristics at Time 1 (see Table 2). These indicated that the distribution of the severity of liver disease, and the proportion of alcoholic cirrhotics, included in the two groups (Tr and LC) were not significantly different.

A total of 12 healthy controls took part in the initial assessment for the study and were contacted, and agreed, to take part in the follow-up study (healthy control group 1). Healthy control group 1 was matched to the liver transplant group by sex, but was poorly matched by age, years in full time education and estimated full scale IQ. A further group of 11 healthy controls (matched by sex, age, years in full time education and estimated full scale IQ) were assessed at the follow-up stage only (healthy control group 2). Refer to Results section, Table 3 for demographic details of groups.

2.3. MEASURES

2.3.1. Demographic Variables

Demographic variables including: sex, age, educational level and estimated full scale IQ were obtained. Details of type and severity of liver disease were also obtained at the initial assessment stage (see Table 2). Severity of liver disease was calculated according to the following criteria: serum albumin level; serum bilirubin level; prothrombin time; presence or absence of encephalopathy; and presence or absence of ascites. Results indicate the level of liver disease as A (mild), B (moderate) or C (severe).

Full scale IQ was estimated by the National Adult Reading Test (NART, Nelson & Willison, 1987). This test is very easy to administer, requiring oral pronunciation of a list of 50 irregular words. It is a particularly good

test to estimate premorbid intelligence levels, being relatively resistant to cognitive impairment. High internal reliability of 0.93 has been reported (Nelson & Willison, 1991), and inter-rater reliability has been found to be equally high between 0.96 and 0.98 (O'Carroll, 1987). Finally, a test-retest reliability co-efficient of 0.98 has been reported (Crawford et al., 1989).

2.3.2. Self-administered questionnaires

2.3.2.1. The Rotterdam Symptom Checklist (RSC, De Haes, 1986, Appendix 3).

Quality of life data were obtained using a modified version of the RSC. This questionnaire was originally developed for use with oncology subjects. It consists of 8 psychological and 19 physical items. The physical component was modified by the present researcher for use with liver disease subjects by extracting oncology-specific items and substituting them with the most commonly reported liver disease-specific physical symptoms. Psychological items were unchanged as they were designed for non-specific illness populations. At the time of the initial recruitment of subjects, use of the RSC with illness populations was recommended by the Medical Research Council (McGuire & Selby, 1989).
Subjects were asked to rate each symptom (psychological and physical) on a 4 point scale (not at all, a little, moderately, very much) according to how they have felt over the past week. Scores of psychological QoL range from 8-19, and scores for physical QoL range from 19-45.

2.3.2.2. The Hospital Anxiety and Depression Scale (HADS, Zigmond & Snaith, 1983, Appendix 4).

This is a well established British scale which has been used as a screening instrument for anxiety and depression in non-psychiatric populations. High internal consistency of the HADS has been reported(Cronbach's

alpha = 0.93 for anxiety and 0.90 for depression, Moorey et al, 1991). It consists of two 7 item scales in which subjects answered questions indicating their response on a 4 point scale. Scores range from 0-21 for anxiety and depression, with a score of 10 or above generally taken as indicative of "caseness".

2.3.2.3. Rosenberg Self-Esteem Scale (RSE, Rosenberg, 1989, Appendix 5).

The RSE is a widely used in healthcare as a measure of global self-esteem. It consists of ten items which the subject is asked to rate on a four point scale. The scores range from 10-40, with a high score indicating high self-esteem. Test-tetest reliability has been reported to be 0.63 (Byrne, 1983).

2.3.2.4. Acceptance of Illness Scale (AIS, Felton et al, 1984, Appendix 6).

The AIS measures the extent to which an individual is able to accept their illness without experiencing negative feelings or responses. The authors (Felton et al., 1984) of the scale have demonstrated high internal consistency (Cronbach's alpha = 0.81 to 0.83) and a reasonably high test-retest reliability over a seven month period (Spearman's rho = 0.69). The scale includes eight items on which subjects rated the extent to which they agree of disagree with statements about their illness on a 5-point scale. This scale was not used with the healthy control groups. Scores range from 8-40, with a high score indicating good acceptance of illness.

2.3.2.5. Significant Others Scale (SOS, Power et al, 1988, Appendix 7).

The SOS is designed to measure the quality of the support provided by significant others in an individual's social network. Test-retest reliability across the scores of social support over a six-month interval ranged from 0.73 to 0.83 (Power et al, 1988; Power & Champion, 1992). Subjects were asked to specify up to seven important people in their lives and then

asked to rate, on a seven point scale, two questions on the level of emotional and then practical support that each person provides. Subjects were also asked to rate the ideal levels of emotional and practical support wished for each person specified. The discrepancy between actual and ideal support for each person specified can then be calculated. Mean scores for actual and ideal, emotional and practical support range from 1-7.

2.3.3. Repeated Neuropsychological Measures

2.3.3.1. Rivermead Behavioural Memory Test (RBMT, Wilson et al, 1989).

The RBMT is a valid measure of everyday memory difficulties which includes four matched parallel versions to control for practice effects. Two parallel versions were used in the present study, at Time 1 and Time 2. It consists of a number of sub-tests designed to map directly onto a component of everyday memory. Scores range from 0-24.

2.3.3.2. The Digit Span subtests of the Wechsler Adult Intelligence Scale - Revised (DF & DB, Wechsler, 1981).

This subtest comprises two components, Digits Forward and Digits Backward. Both tests involved the administration of two trials for each span length of a series of random numbers. Digits Forward span length ranges from three to nine consecutive numbers, and Digits Backward two to eight consecutive numbers. Both tests measure auditory attention and immediate verbal recall, although Digits Forward involves a larger component of efficiency of attention, and Digits Backwards is a more demanding task and involves a larger component of working memory. Both tasks have been shown to be sensitive to brain damage, although Digits Backwards is more so (Lezak, 1983, pp266-270). For each subtest, scores range from 0-14.

2.3.4. Neuropsychological measures assessed at Time 2 only.

The neuropsychological functions assessed at Time 1 were limited to attention and memory. In order to extend the range of neuopsychological functions assessed, two further tests were added at Time 2. The Digit Symbol Substitution Test was included to measure psychomotor performance, and verbal fluency was added to measure executive functioning.

2.3.4.1. The Digit Symbol Substitution Test of The Wechsler Adult Intelligence Scale - Revised (DSST, Wechsler, 1981).

This test consists of a series of small blank boxes paired to a randomly assigned number from one of nine. Each number is matched to a symbol, and the subject is asked to fill in the corresponding symbol, paired to each number, in the boxes as quickly as possible. The subject is stopped after 90 seconds. This test measures psychomotor performance, and is relatively unaffected by memory and learning (Lezak, 1983, p273). It has been shown to be particularly sensitive to even minimal brain damage (Hirschenfang, 1960). Further, this test is particularly sensitive to the cognitive impairment associated with liver disease (O'Carroll et al., 1991). Scores range from 0-93.

2.3.4.2. Verbal Fluency Test (VFT, Benton et al, 1983)

Verbal fluency is the speed and ease of verbal production and is a measure of executive functioning. It is most commonly measured by word naming tests. The most common format involves three word-naming trials in which the subject is asked to name as many words as possible beginning with the letters FAS. This test has proven to be a sensitive indicator of brain dysfunction (Benton, 1968).

2. 4. PROCEDURE

At the initial assessment stage (Time 1), all tests and questionnaires were administered to subjects during an interview at the Royal Infirmary of Edinburgh. The interview lasted between 1 and 2 hours and the tests were administered in the following order: RBMT; DF, DB; HAD, RSC.

At the follow-up stage (Time 2), the self-administered questionnaires were sent by post (see section 2.3.2.). The neuropsychological assessment was carried out during an interview with the researcher either at the Royal Infirmary of Edinburgh or at the subject's home (see sections 2.3.3. and 2.3.4). The interview lasted approximately 1 hour and the tests were administered in the following order: RBMT; DF, DB; verbal fluency; and DSST.

CHAPTER 3: RESULTS

3.1. DEMOGRAPHIC DATA

Table 3: Demographic characteristics of groups

Variable		Trans-plant group (Tr) (N=16)	Liver control group (LC) (N=11)	Healthy control group1 (HC1) (N=11)	Healthy control group2 (HC2) (N=12)	F	p	Scheffé P<0.05
Sex	Male	6	4	3	7	x=6.7	0.35	-
	Female	10	7	8	5			
Age (Years)	Mean (SD)	48.9 (12.4)	52.3 (13.3)	27.0 (9.8)	42.9 (13.2)	9.5	0.001	HC1<Tr, LC, HC2
Years in Educ.	Mean (SD)	11.8 (3.6)	11.3 (2.9)	16.3 (1.7)	14.5 (2.8)	7.4	0.004	HC1<Tr, LC, HC2
Full Scale IQ	Mean (SD)	100.9 (12.73)	102.2 (11.63)	111.6 (7.3)	106.9 (9.6)	2.5	0.074	-
Months between Assess-ments	Mean (SD)	35.8 (4.9)	35.2 (6.5)	49.1 (5.8)	NA*	22.6	0.000	HC1<Tr, LC

* NA = not applicable

Demographic data on subjects in the four groups (Tr, LC, HC1 and HC2) are presented in Table 3.

One-way ANOVAs, with four groups, indicated that there were significant between group differences in age, years in education and months between assessments (Table 3). To establish which groups were different, Scheffé tests, (significance level, $p < 0.05$), were used, which significantly differentiated the healthy control group 1 from the other groups on these variables. There were no significant differences in sex (using a Chi squared test) or full scale IQ between any of the groups. The transplant group (Tr), the liver control group (LC) and the healthy control group 2 (HC2) were not significantly different on any of these measures.

3.2. Repeated Measures Analyses

These analyses included three groups: liver transplant group (Tr); liver disease control group (LC); and healthy control group 1 (HC1). Repeated measures analyses included two time points: initial assessment (Time 1); and follow-up assessment (Time 2).

3.2.1. Quality of life

3.2.1.1. Psychological Component

A repeated measures analysis of variance (ANOVA), with two time points and three groups, indicated that there was a significant, overall difference in psychological quality of life between the three groups. Examination of the means indicated that the healthy control group had a better psychological QoL than both of the liver disease groups (see Table 4).

Table 4: Change in scores of psychological component of QoL.

Group	Time 1 Mean (SD)	Time 2 Mean (SD)
Liver Transplant	17.4 (4.6)	15.5 (6.0)
Liver Control	14.7 (4.4)	15.8 (7.3)
Healthy Control 1	12.1 (2.9)	11.2 (2.4)

Group Effect F=4.38, p=0.020
Time Effect F=0.37, p=0.547
Interaction F=0.91, p=0.412

There was, however, no effect of time and no interaction between the groups over time. It is notable that the largest change in scores over time was the improvement in scores of the transplant group.

Comparison of means at Time 2

All four groups were compared at Time 2 to assess whether the psychological QoL of transplant recipients 3 years post-transplant was different to that of healthy or liver disease controls. A one-way ANOVA, with four groups (including healthy control group 2), indicated that no two groups were significantly different on scores of psychological QoL at Time 2 (see Table 5).

Table 5: Comparison of groups on repeated measures at Time 2.

Measure	Trans-plant group Mean(SD)	Liver control group Mean(SD)	Healthy control group 1 Mean(SD)	Healthy control group 2 Mean(SD)	F	p	Scheffé p<0.05
Psycho-logical QoL	15.5 (6.0)	14.7 (6.6)	11.2 (2.4)	13.5 (3.8)	1.72	0.1774	-
Physical QoL	31.6 (9.4)	40.2 (14.5)	22.3 (2.2)	27.3 (6.6)	7.25	0.0005	LC>HC1, HC2
Anxiety	5.9 (4.1)	5.2 (5.7)	4.5 (3.9)	6.8 (3.4)	0.60	0.620	-
De-pression	3.5 (3.2)	4.6 (4.2)	0.9 (1.8)	2.5 (2.6)	2.86	0.047	-
Memory (RBMT)	20.4 (2.7)	18.8 (3.7)	21.2 (1.8)	21.5 (3.0)	1.92	0.164	-
Digits Forward	8.0 (2.5)	9.7 (3.3)	10.5 (1.7)	10.8 (2.1)	3.44	0.025	-
Digits Backward	6.7 (2.8)	7.9 (3.0)	8.5 (2.5)	8.8 (2.2)	1.61	0.2023	-

3.2.1.2. Physical Component

A repeated measures ANOVA, with two time points and three groups, indicated that there was a significant overall difference in physical quality of life between the groups (see Table 6). Again, examination of the means indicated that the healthy control group had a better physical QoL compared with both of the liver disease groups.

Table 6: Change in scores of physical component of QoL.

Group	Time 1 Mean (SD)	Time 2 Mean (SD)
Liver Transplant	34.9 (7.9)	31.6 (9.4)
Liver Control	40.2 (11.9)	40.91 (14.0)
Healthy Control 1	23.0 (2.9)	22.3 (2.2)

Group Effect F=13.03, p=0.000
Time Effect F=0.61, p=0.440
Interaction F=0.75, p=0.478

There was no effect of time and there was no interaction between the groups over time, although the largest change in scores was the improvement in scores of the transplant group.

Comparison of means at Time 2

A one-way ANOVA, with four groups (including healthy control group 2), indicated that there was a significant difference between the groups on scores of physical QoL (see Table 5). A Scheffé test, $p<0.05$, indicated that the physical QoL of the liver disease control group was significantly worse than that of both of the healthy control groups. The liver transplant group did not differ significantly from any group 3 years post-transplant.

3.2.2. Anxiety

A repeated measures ANOVA, with two time points and three groups, indicated that there was no significant overall difference in anxiety between the groups (see Table 7).

Table 7: Change in scores of anxiety.

Group	Time 1 Mean (SD)	Time 2 Mean (SD)
Liver Transplant	7.5 (4.6)	5.9 (4.1)
Liver Control	6.3 (3.8)	5.8 (4.7)
Healthy Control 1	5.6 (3.0)	4.6 (3.9)

Group Effect F=0.63, p=0.537
Time Effect F=2.05, p=0.161
Interaction F=0.25, p=0.781

There was no effect of time and there was no interaction between the groups over time. Again, however, the largest change in scores over time was the improvement in scores of the transplant group.

Comparison of means at Time 2

All four groups were compared at Time 2 to assess whether anxiety scores of transplant recipients (3 years post-transplant) were different to those of healthy or liver disease controls (HC1, HC2 and LC). A one-way ANOVA,

with four groups (including healthy control group 2), indicated that no two groups were significantly different on scores of anxiety at Time 2 (see Table 5).

3.2.3. Depression

A repeated measures ANOVA, with 2 time points and 3 groups, indicated that there was a significant overall difference in depression between the groups (see Table 8). Examination of the means indicated that the healthy control group was less depressed than both of the liver disease groups.

Table 8: Change in scores of depression.

Group	Time 1 Mean (SD)	Time 2 Mean (SD)
Liver Transplant	5.2 (3.9)	3.5 (3.3)
Liver Control	4.7 (5.0)	5.2 (4.4)
Healthy Control 1	1.6 (1.7)	0.9 (1.8)

Group Effect F=4.65, p=0.016
Time Effect F=1.18, p=0.284
Interaction F=1.24, p=0.303

There was no overall change over time and there was no interaction between the groups over time. Again, the largest change in scores over time was the improvement in scores of the transplant group.

Comparison of means at Time 2

All four groups were compared at Time 2 to assess whether depression scores of transplant recipients (3 years post-transplant) were different to those of healthy or liver disease controls. A one-way ANOVA, with four groups (including healthy control group 2), indicated that there was a significant overall difference in scores of depression between the groups (see Table 5). A Scheffé test, $p<0.05$, however, indicated that no groups differed significantly from each other.

3.2.4. Neuropsychological Measures

3.2.4.1. Memory - Rivermead Behavioural Memory Test

A repeated measures ANOVA, with two time points and three groups, indicated that there was a significant overall difference in memory between the groups (see Table 9). Examination of the means indicated that the healthy control group scored higher than both of the liver disease groups.

Table 9: Change in scores of memory (RBMT).

Group	Time 1 Mean (SD)	Time 2 Mean (SD)
Liver Transplant	16.7 (3.17)	20.4 (2.7)
Liver Control	17.9 (3.6)	18.8 (3.7)
Healthy Control 1	21.0 (1.4)	21.2 (1.9)

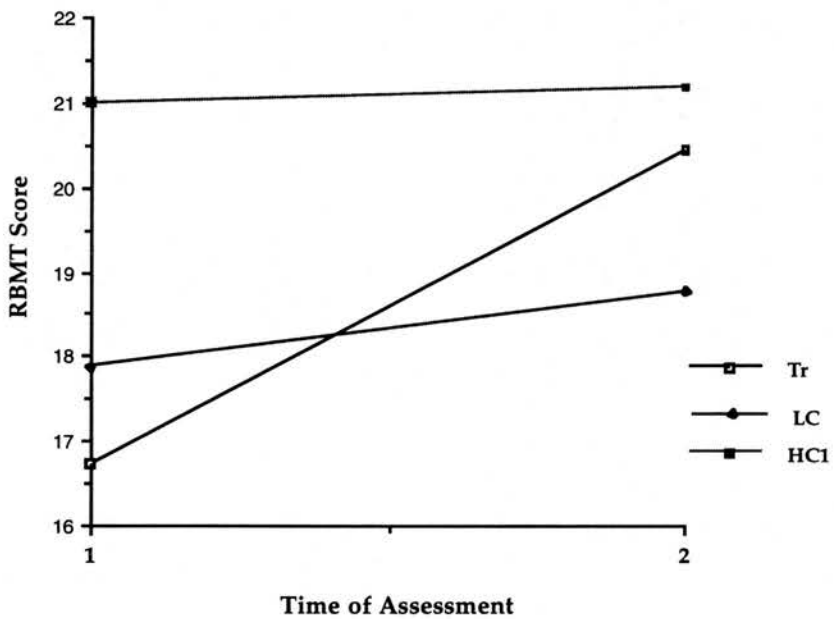
Group Effect F=5.79, p=0.007
Time Effect F=5.88, p=0.021
Interaction F=3.07, p=0.061

There was a significant overall improvement in scores over time, and an interaction between the groups was verging on significance. To investigate the change in scores over time, 2-tailed, related t-tests were carried out for each group (see Table 10). These indicated that the memory functioning of the transplant group had significantly improved at time 2 compared to time 1. No significant improvements were noted for the liver disease control group and the healthy control group (see Figure 1).

Table 10: t Values for within-group differences in memory scores.

Subject Group	t value	p
Transplant Group	2.96	0.011
Liver Disease Control Group	0.69	0.509
Healthy Control Group	0.32	0.756

Figure 1: Change in memory function over time.



Comparison of means at Time 2

All four groups were compared at Time 2 to assess whether the memory functioning of transplant recipients (3 years post-transplant) was different to that of healthy or liver disease controls. A one-way ANOVA, with four groups (including healthy control group 2), indicated that no two groups were significantly different on scores of memory functioning at Time 2 (see Table 5).

3.2.4.2. Digits Forward

A repeated measures ANOVA, with 2 time points and 3 groups, indicated that there was a significant overall difference between the groups on digits forwards (see Table 11). Examination of the means indicated that the healthy control group performed better on this task than both of the liver disease groups.

Table 11: Change in scores of digits forward.

Group	Time 1 Mean (SD)	Time 2 Mean (SD)
Liver Transplant	7.3 (1.9)	8.0 (2.5)
Liver Control	8.1 (2.03)	9.7 (3.3)
Healthy Control 1	10.8 (1.7)	10.5 (1.7)

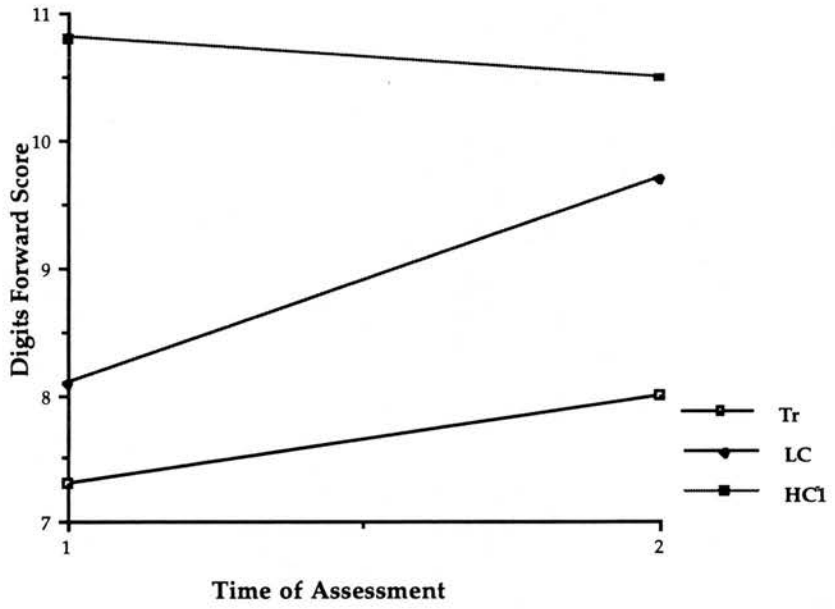
Group Effect F=6.38, p=0.005
Time Effect F=5.17, p=0.030
Interaction F=3.62, p=0.039

There was a significant overall effect of time and a significant interaction between the groups. To determine the nature of this interaction, 2-tailed, related t-tests were carried out for each group (see Table 12). These indicated that the change in scores of digits forward of the liver disease control group was verging on a significance. No significant improvements were noted for the transplant group and the healthy control group (see Figure 2).

Table 12: t Values for within-group differences in digits forward scores.

Subject Group	t value	p
Transplant Group	1.55	0.146
Liver Disease Control Group	2.26	0.054
Healthy Control Group	1.49	0.167

Figure 2: Change in scores of digits forward over time.



Comparison of means at Time 2

All four groups were compared at Time 2 to assess whether the performance on digits forward of transplant recipients (3 years post-transplant) was different to that of healthy or liver disease controls. A one-way ANOVA, with four groups (including healthy control group 2), indicated that there was a significant overall difference between the groups

on digits forward performance (see Table 5). A Scheffé test, $p<0.05$, however, indicated that no groups differed significantly from each other.

3.2.4.3. Digits Backward

A significant overall difference between groups was indicated by a repeated measures ANOVA, with two time points and three groups. Examination of the means indicated that the healthy control group performed better than the liver disease groups at digits backward (see Table 13).

Table 13: Change in scores of digits backward.

Group	Time 1 Mean (SD)	Time 2 Mean (SD)
Liver Transplant	4.8 (2.2)	6.7 (2.8)
Liver Control	6.6 (2.0)	7.9 (3.0)
Healthy Control 1	9.1 (2.1)	8.5 (2.5)

Group Effect F=5.02, p=0.013
Time Effect F=8.54, p=0.006
Interaction F=7.19, p=0.003

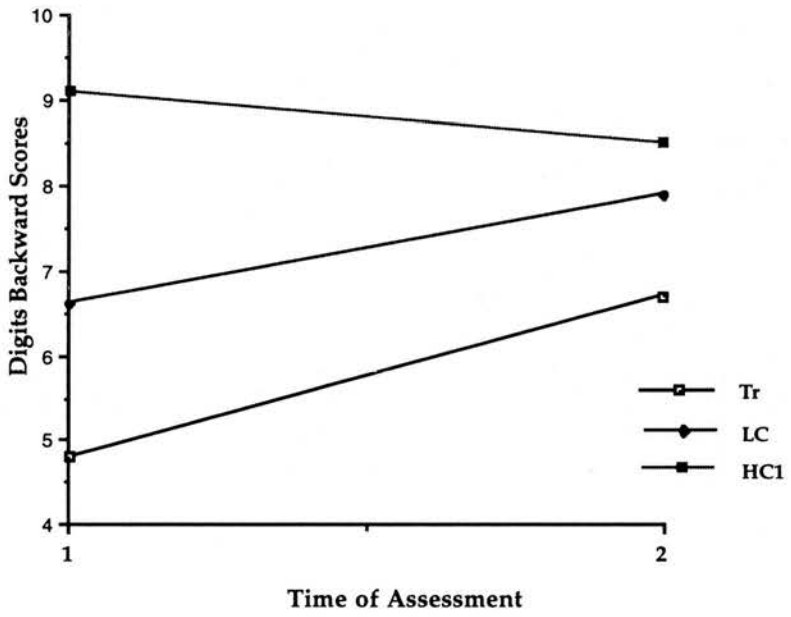
A significant overall effect of time, and a significant interaction between the groups were found. To determine the nature of the interaction, 2-tailed, related t-tests were carried out for each group (see Table 14). These indicated that the transplant group showed a highly significant improvement on digits backward at time 2 compared to time 1. No

significant improvements were noted for the liver disease control group and the healthy control group (see Figure 3).

Table 14: t Values for within-group differences in digits backward scores.

Subject Group	t value	Significance
Transplant Group	4.68	0.0004
Liver Disease Control Group	1.67	0.134
Healthy Control Group	1.75	0.111

Figure 3: Change in scores of digits backward over time.



Comparison of means at Time 2

All four groups were compared at Time 2 to assess whether the performance on digits backwards of transplant recipients (3 years post-

transplant) was different to that of healthy or liver disease controls. A one-way ANOVA, with four groups (including healthy control group 2), indicated that no two groups were significantly different on performance on digits backward at Time 2 (see Table 5).

3.3. ANALYSIS OF MEASURES USED AT TIME 2 ONLY (DSST, VF, RSE, AOI, SOS)

The second healthy control group (healthy control group 2, matched to the liver transplant group on age, years in education and estimated full scale IQ, as well as sex, see Table 3) was included in these analyses.

3.3.1. Neuropsychological Measures

3.3.1.1. Verbal Fluency

A one-way ANOVA indicated that there was a significant overall difference between the groups on the verbal fluency task (see Table 15). A Scheffé test (with significance level $p<0.05$) was carried out to determine the nature of this difference. This showed that both of the healthy control groups performed significantly better than the liver disease groups. The liver disease groups did not differ significantly from each other.

Table 15: Means and F values for measures used at Time 2 only

Measure	Trans-plant group Mean(SD)	Liver control group Mean(SD)	Healthy control group 1 Mean(SD)	Healthy control group 2 Mean(SD)	F	p	Scheffé p<0.05
Verbal fluency	33.1 (10.9)	31.2 (7.7)	49.5 (13.6)	47.3 (11.2)	7.97	0.0003	HC1, HC2 > Tr, LC
DSST	43.9 (13.4)	37.3 (15.2)	69.5 (7.9)	62.4 (8.8)	18.33	0.0000	HC1, HC2 > Tr, LC
Self-esteem	19.3 (6.6)	19.8 (8.1)	16.9 (4.2)	20.8 (4.0)	0.88	0.4584	-
Acc. of illness	28.3 (8.7)	27.3 (8.7)	-	-	0.07	0.80	-

3.3.1.2. Digit Symbol Substitution Test

A one-way ANOVA indicated that there was a highly significant overall difference between the groups on the DSST (see Table 15). A Scheffé test (with significance level $p<0.05$) showed that both of the healthy control groups performed significantly better than the liver disease groups. The liver disease groups did not differ significantly from each other.

3.3.2. Acceptance of Illness

A one-way ANOVA indicated that there were no overall differences between the liver disease groups on the Acceptance of Illness scale (see Table 15). The scores for both groups (Tr and LC) fell within the range of good acceptance of illness.

3.3.3. Self-Esteem

A one-way ANOVA indicated that there were no overall differences between the four groups on the RSE (see Table 15). All Four groups (Tr, LC, HC1 and HC2) reported high self-esteem.

3.3.4. Social Support

One-way ANOVAs indicated that there were no differences between the groups on any component of social support measured (see Table 16).

Table 16: Means and F values for social support.

Social support	Transplant group Mean (SD)	Liver control group Mean (SD)	Healthy control group 1 Mean (SD)	Healthy control group 2 Mean (SD)	F	p
Actual emotional support	5.7 (0.9)	6.0 (0.9)	6.6 (2.9)	5.5 (0.9)	1.03	0.389
Ideal emotional support	6.2 (0.6)	6.7 (1.0)	6.2 (0.5)	6.2 (0.5)	1.86	0.151
Discrepancy - emotional support	0.6 (0.5)	0.8 (0.8)	0.5 (0.5)	0.7 (0.7)	0.37	0.776
Actual practical support	5.7 (1.0)	5.6 (1.4)	5.7 (0.6)	5.4 (1.0)	0.22	0.884
Ideal practical support	5.9 (0.6)	6.2 (1.1)	6.1 (0.5)	6.0 (0.7)	0.33	0.801
Discrepancy - practical support	0.3 (0.5)	0.8 (0.8)	0.5 (0.4)	0.6 (0.6)	1.37	0.266

All groups (Tr, LC, HC1 and HC2) were receiving adequate emotional and practical support.

In order to investigate the relationships between discrepancies in actual and ideal levels of social support, and quality of life, anxiety and depression, Pearson correlations were carried out (see Table 17). A significant positive correlation between anxiety and discrepancy between actual, and ideal, practical support was found. A positive correlation between anxiety and discrepancy between actual, and ideal, emotional support was verging on significance.

Table 17: Correlations between discrepancies in actual and ideal levels of social support and QoL, anxiety and depression.

Variable	Discrepancy in emotional support	Discrepancy in practical support
Psychological QoL	-0.02	0.00
Physical QoL	0.18	0.19
Anxiety	0.28 **	0.30 *
Depression	0.22	0.18

* = significant at $p<0.05$

**= significant at $p<0.06$

CHAPTER 4: DISCUSSION

4.1. SUMMARY OF RESULTS

As the present study included multiple variables, a summary of the results will be presented to aid the reader's interpretation of the main findings of the study.

4.1.1. Demographic Data

There were no differences between the four groups in distribution of sex (Table 3). The liver disease groups (Tr & LC) and the second healthy control group (HC2, assessed at time 2 only) were also well matched on age, years in full time education and estimated full scale IQ. The repeated measures healthy control group (HC1) was poorly matched to the transplant group on these measures. Their inclusion in the study was to control for repeated testing effects.

4.1.2. Quality of Life

The hypotheses indicated that there would be an interaction between the three repeated measures groups (Tr, HC1 and LC) as follows: the transplant group would show improved physical and psychological components of QoL; the liver disease control group would show a deterioration in physical and psychological QoL; and the healthy control group would demonstrate no change in either of the components.

Significant overall between group differences in both physical and psychological QoL indicated that the healthy control group (HC1) had a better QoL than both of the liver disease groups (Tr and LC, Tables 4 and 6). None of the groups changed significantly over time. The psychological

and physical QoL of the liver transplant group did not differ significantly from either the liver disease controls or the healthy controls post-transplant. At the follow-up assessment time, the physical QoL of the liver disease controls was significantly poorer than the healthy controls (Table 5).

4.1.3. Anxiety and Depression

The hypotheses indicated that there would be an interaction between the three repeated measures groups (Tr, HC1 and LC) as follows: the transplant group would show improved anxiety and depression; the liver disease control group would show a deterioration in anxiety and depression; and the healthy control group would demonstrate no change in either anxiety or depression.

Analysis of the results indicated that there were no overall differences in anxiety between the groups (Tr, LC and HC1, Table 7). The healthy control group (HC1) were significantly less depressed than the liver disease groups (Tr and LC, Table 8). There were no significant changes in anxiety or depression over time in any group.

4.1.4. Neuropsychological Measures

4.1.4.1. Rivermead Behavioural Memory Test

The hypotheses indicated that there would be an interaction between the three repeated measures groups (Tr, HC1 and LC) as follows: the transplant group would show improved memory; the liver disease control group would show a deterioration in memory; and the healthy control group would demonstrate no change in memory.

Analysis of the results indicated that there was a significant overall difference in memory between the groups (Tr, LC and HC1, Table 9). The healthy control group demonstrated significantly better memory function than the liver disease groups. There was a significant overall improvement with time, and the interaction between the groups was verging on significance. Further analysis indicated that the improvement in memory function of the transplant group was highly significant, whereas the slight improvements noted by both of the other groups were not (Table 10).

In conclusion, the memory function of the transplant recipients improved over time to the level of the healthy population.

4.1.4.2. Digits Forward

The hypotheses indicated that there would be an interaction between the three repeated measures groups (Tr, HC1 and LC) as follows: the transplant group would show improved performance; the liver disease control group would show a deterioration in performance; and the healthy control group would demonstrate no change in performance.

Analysis of the results indicated that there was an overall difference in performance between the groups (Table 11). The healthy control group (HC1) performed significantly better at this task than the liver disease groups (Tr and LC). There was also a significant overall improvement in performance over time. An interaction between the groups over time was also significant, and further analysis indicated that the improvement in performance of the liver disease control group was verging on significance (Table 12).

4.1.4.3. Digits Backward

The hypotheses indicated that there would be an interaction between the three repeated measures groups (Tr, HC1 and LC) as follows: the transplant group would show improved performance; the liver disease control group would show a deterioration in performance; and the healthy control group would demonstrate no change in performance.

Analysis of the results indicated that there was a significant overall difference in performance between the groups (Table 13). The healthy control group (HC1) performed better than the liver disease groups (Tr and LC). There was a significant overall improvement with time, and an interaction between the groups was also significant. Further analysis indicated that the improvement in performance of the transplant group was highly significant, whereas the slight improvement noted by the liver disease control group, and slight deterioration of the healthy control group (HC1) were not (Table 14).

4.1.4.4. Verbal Fluency

The hypotheses indicated that the liver transplant group (Tr) would perform at the same level as the healthy control groups (HC1 and HC2), which would be better than the liver disease control group (LC).

A significant overall difference was found between the four groups (Table 15). Further analysis indicated that both of the healthy control groups (HC1 and HC2) performed significantly better than both of the liver disease groups (Tr and LC). There was no difference between the transplant group and the liver disease control group.

4.1.4.5. Digit Symbol Substitution Test

The hypotheses indicated that the liver transplant group (Tr) would perform at the same level as the healthy control groups(HC1 and HC2), which would be better than the liver disease control group (LC).

A highly significant overall difference was found between the four groups (Table 15). Further analysis indicated that both of the healthy control groups (HC1 and HC2) performed significantly better than both of the liver disease groups (Tr and LC). There was no difference between the transplant group and the liver disease control group.

4.1.5. Acceptance of Illness Scale

The hypotheses stated that the liver transplant group (Tr) would have a more positive acceptance of their illness than the liver disease control group (LC).

No significant difference was found in acceptance of illness between the two groups (Table 15).

4.1.6. Rosenberg Self Esteem Scale

The hypotheses stated that the liver transplant group (Tr) would have equivalent self esteem levels to the healthy control groups (HC1 and HC2), which would be higher than that of the liver disease control group (LC).

No differences in self esteem were found between the four groups (see Table 15).

4.1.7. Social Support

The hypotheses stated that discrepancies in social support would be higher for both of the liver disease groups (Tr and LC), as their ideal levels of support would be higher. It was also stated that discrepancies in emotional or actual social support would be related to poorer QoL and higher anxiety and depression.

No differences in actual, ideal or discrepancies between the two, in both emotional and practical support, were found between the four groups (see Table 16). Significant correlations indicated that the greater the discrepancy between actual and ideal emotional and practical support, the higher the anxiety reported (see Table 17). No significant correlations were found between discrepancies and depression or QoL.

4.2. Selection Bias

It may have been the case that selection bias influenced the results. Of the original 50 liver disease controls considered for repeat assessment, 28 had died before the follow-up assessment and a further 11 failed to respond to the request to take part in the follow-up assessment. It may have been that those included in the follow-up liver disease control group were those most well. This would have positively skewed the results. Indeed, all those who took part were living independently at home. Nevertheless, the same selection bias may have been true for the liver transplant group. An overall selection bias in both liver disease groups stems from their inclusion in the original assessment. This involved a selection bias given that those who were too ill were not included as the assessment had to take place up one flight of stairs, with no access to a lift.

4.3. COMPARISON WITH OTHER STUDIES

There can only be a limited comparison to previous work as the present study appears to be the first controlled study in this area that uses repeated analyses of pre- and post-transplant data.

4.4. SUPPORT FOR EACH HYPOTHESIS (refer to section 1.13).

4.4.1. Liver transplant recipients will have improved on mood (anxiety and depression), quality of life and neuropsychological measures.

Essentially, the most striking overall result from the present study is the limited extent to which this hypothesis has been supported.

4.4.1.1. Quality of Life

The psychological and physical QoL of transplant recipients had not improved significantly compared to pre-transplant levels (Tables 4 and 6). Although there was no significant effect of time on the QoL of transplant recipients, there were no significant differences in psychological QoL between any of the groups (Tr, LC, HC1 and HC2) at Time 2 (Table 5). The physical QoL of the transplant recipients did not differ significantly from the healthy control groups or the liver disease control group at Time 2 (Table 5). There was, however, high variance in scores of both psychological and physical QoL, and it remains to be seen whether significant differences would be found with larger samples. With both psychological and physical QoL components non-significant trends towards improved QoL were found. With larger samples, it would be hoped that the changes would be significant. The limitations of the questionnaire used to assess QoL in the present study, the Rotterdam Symptom Checklist, must be noted. At the initial recruitment time of the study, the use of this measure was recommended by the Medical Research

Council (McGuire & Selby, 1989). The measure is very easy to administer and complete, which is crucial in longitudinal designs, which rely on subjects agreeing to repeat assessments. It is, however, a fairly specific measure, and the physical component used in the present study was modified for use with liver disease patients. It may be that a more generic item would have produced different results. Since that time other measures have been developed, particularly the WHOQOL (WHOQOL group, 1994), which was designed as an international, multidimensional, generic instrument for use in health care. This measure would be the measure of choice in future studies. Nevertheless, the present study supports similar findings by Tarter et al. (1984), who reported no difference in QoL between liver transplant recipients three years post-transplant and a control group of Crohn's disease patients, using the Sickness Impact Profile (SIP). Unfortunately, no healthy control group was included in the study. Collis et al. (1995) reported improved levels of QoL (although no repeated measures analysis was carried out), measured by the Nottingham Health Profile (NHP), in a sample of 10 liver transplant recipients (between 2 and 151 weeks post-transplant), although not to the levels of the general population. No control group was included in the study, and the variance in time between transplant and follow-up assessment was large, thus limiting the interpretation of the results. It is clear that further investigation of the QoL outcome of liver transplantation is needed. In particular, prospective, well controlled studies using standardised instruments with larger sample sizes are required.

4.4.1.2. Mood

Again, the intervention of liver transplantation did not significantly effect the anxiety or depression levels of transplant recipients (Tables 7 and 8). There were, however, no overall differences in anxiety levels between the transplant group and the healthy controls or the liver disease control group. In contrast other studies have found elevated anxiety levels of

liver transplant recipients even years after transplantation (Kuchler et al., 1991; Reither et al., 1992). Transplant recipients and liver disease controls were, however, overall significantly more depressed than healthy controls (HC1). In a retrospective study assessing the psychosomatic aspects of liver transplantation, Surman et al. (1987) noted that 8/40 post-transplant patients were referred for treatment for depressive symptoms. Further, Sarin et al. (1988) found that a quarter of patients interviewed after transplantation reported levels of anxiety or depression.

Collis et al. (1995) reported that there were no significant changes in levels of anxiety and depression (measured by the General Health Questionnaire) in a group of 11 transplant recipients, assessed pre- and between 2 and 151 weeks post-transplant. Unfortunately there were no control groups included in the study for comparison. Cross-sectional analyses of mood post-transplant have found elevated levels of anxiety and depression in liver transplant recipients. Hicks et al. (1992), found that levels of depressed and anxious mood were higher in patients greater than 2 years post-transplant compared to a group less than 2 years post-transplant. Tarter et al. (1984) assessed a group of 10 liver transplant recipients 3 years post-transplant and found that they displayed moderate anxiety, somatic distress and concern, frustration, depression, worry and social withdrawal, compared to population norms. They found no difference between transplant patients and a matched group of patients with Crohn's disease.

One explanation for the elevated anxiety and depression levels found in transplant recipients in other studies is that the measures used to assess mood were not designed for use with physically ill populations and therefore the results reported in the study may be skewed. In the present study, small sample sizes and high variability within groups may have masked differences between groups, and changes over time that may have been significant in a larger sample size. It is clear, again, that further investigation of the impact that liver transplantation has on the levels of

anxiety and depression of patients is required. Without pre-transplant data and comparison to well matched controls, cross-sectional studies measuring mood post-transplant provide little information. The only two prospective studies in this area (the present study and Collis et al., 1995) have found that liver transplantation has no effect on anxiety and depression levels.

4.4.1.3. Memory

The significant improvements in memory (measured by the Rivermead Behavioural Memory Test) of the liver transplant recipients following transplantation was the most notable result of the present study (Tables 9 and 10). Within memory functioning categories of normal, poor, moderate impairment and severe impairment specified by the RBMT, the memory functioning of the liver transplant group at the pre-transplant assessment stage fell within the level of moderate impairment on the RBMT. At the post-transplant stage, transplant recipients were performing within the level of poor memory functioning, although it must be noted that the performance of both of the healthy control groups was also within the level of poor memory functioning as categorised by the RBMT. It may be that as samples vary, so do the boundaries between the categories of memory functioning specified by the RBMT. Nevertheless, the change in memory functioning of the liver transplant group was clinically significant. Indeed, at the follow-up assessment there were no significant differences between the liver transplant group and the healthy control group (Table 5), indicating that at three years post-transplant the memory function of transplant recipients is largely restored to that of a group of matched healthy controls. This supports the findings of improvement in memory functioning of 62 subjects following liver transplantation by Tarter et al (1990a).

The finding that liver transplantation was associated with a highly significant improvement on the digits backward task is further evidence that memory functioning of transplant recipients was improved post-transplant (Table 13). There was no significant improvement by the transplant group on the digits forward task (Tables 11 and 12), and there was a significant overall difference in performance between the groups at the post-transplant stage, although no groups differed significantly from each other (Table 5). As well as a memory component, digits forward also involves a large element of efficiency of attention. The lack of improvement on the digits forward task of the transplant recipients indicated that the significant improvement found on the RBMT cannot be explained by improved attention post-transplant.

The impaired performance on digits forward and backward tasks (Tables 11 and 13), compared to the healthy control group (HC1), of both liver disease groups (Tr and LC) in the present study was in contrast to results reported by Tarter et al. (1990a), who found no impairments on digits forward or digits backward in a liver transplant group either pre- or three years post-transplant. Elsass et al. (1978), however, did find that a group of 22 cirrhotics were impaired on the digit span task. Variability within samples may explain these differing results, and therefore the use of the digit span subtests in cross-sectional analyses may not be recommended. The use of the digit span subtests in repeated measures analysis in the present study, however, has provided important evidence of improvements in memory functioning, regardless of attention, 3 years post-transplant.

The significant improvements in memory after liver transplantation found in the present study are particularly important. Individual goals often include returning to work and resuming activities which had not been possible for some time as their liver disease deteriorated prior to the transplant. Memory function can be a vital component to many jobs and

activities. Further, adherence to the strict anti-rejection medication regimens required a good working memory.

4.4.1.4. Executive function and psychomotor speed

In the cross-sectional analysis at Time 2, executive function of transplant recipients, as measured by verbal fluency, was significantly poorer to that of the healthy control groups (HC1 and HC2, Table 15). There was no difference in performance on the verbal fluency task between the liver transplant group and the liver disease control group. Impairment on verbal fluency in a group of 22 cirrhotics was also found by Elsass et al. (1978). The same pattern of results was found for performance on the digit symbol substitution test (Table 15), which measures psychomotor speed and is particularly sensitive to the cognitive impairment associated with liver disease (O'Carroll et al., 1991, Gitlin et al., 1986). The findings that there were no differences between the two liver disease groups on these tasks (VF and DSST) is important, and suggests that the functions being measures by these tasks are less reversible than other neuropsychological impairments associated with chronic liver disease. It may be that these functions take longer to return post-transplant than memory and attention. Alternatively, it may be that these impairments in the transplant recipients reflect permanent cerebral damage. Interestingly, the finding that impairment on the DSST task endures following a liver transplant was also found by Tarter et al. (1990a). In a larger sample (N=62), the DSST was one of only four out of 26 tasks remaining impaired three years post-transplant, although no repeated measures analysis was included in the study to assess whether there had been any change over time. Finally, it may be that the neuropsychological functions measured by these tasks are impaired by the medication that the liver transplant recipients are taking. Motor tremor, for example, has been noted to be a side-effect of immunosuppressant medication (Tarter et al., 1990a). The DSST task tests psychomotor speed, and therefore may be particular

sensitive to these effects. The lack of pre-transplant data on these tasks in the present study must be acknowledged, and limits the interpretation of the results given that data on any improvements or deterioration in functioning are lacking.

4.4.2. The liver disease control group will have deteriorated on mood, quality of life and neuropsychological measures.

Another striking result of the present study is the minimal support for this hypothesis, and indeed in many cases the improved functioning found in this group after an interval of three years. As expected, the liver disease control group had significantly poorer overall physical and psychological quality of life than healthy controls (HC1), but no change had occurred over time (Tables 4 and 6). There were no differences in anxiety levels between the groups (Tr, LC and HC1), and again anxiety levels of the liver disease control group did not change over time (Table 7). Overall, the liver disease control group were significantly more depressed than healthy controls (HC1), and although there was an overall significant difference between the groups at Time 2, no groups differed significantly from each other (Table 5). Again, there was no change in levels of depression in the liver disease controls over time (Table 8). Importantly, there was no deterioration on any measure of neuropsychological functioning of the liver disease control group over time (Tables 9-14). In fact, the performance of the liver disease control group on the digits forward task improved over time to a level verging on significance (Table 10).

In summary, the only measure which differentiated the liver disease controls from the liver transplant recipients at Time 2 was the physical component of QoL (Table 5).

4.4.3. The healthy control group (1) will show no change on mood, quality of life and neuropsychological measures.

This hypothesis was supported on all the measures included in the present study. The time between the assessments was lengthy, and where possible, parallel versions of tests were used, thus minimising an effect of repeat testing. Although the repeated measures control was poorly matched to the liver disease groups, its inclusion was useful by allowing the elimination of repeat testing affects. Further, healthy control group 1 did not differ from healthy control group 2 (well-matched to the liver disease group) on any measure included in the present study.

4.4.4. Self-esteem of liver transplant recipients will match that of healthy controls, whereas liver disease controls will have lowered self-esteem.

A clearly unexpected finding was that there were no differences between the four groups (Tr, LC, HC1 and HC2) in self-esteem, with all groups reporting high self-esteem (Table 15). The measure used to assess self-esteem is one commonly used in health psychology, therefore designed to target components of self-esteem that can be affected by health problems. Wolcott et al. (1989), using a different measure, Simmons Scale of self-esteem, also reported high self-esteem in a group of 41 liver transplant recipients. What is also notable is that the mean levels of self-esteem found in the present study samples are very different to those reported in a normal population sample of 2,294 North American men and women between the ages of 18 and 65 using the Rosenberg Self-Esteem Scale (mean=34.7 (sd=4.9), Rosenberg, 1989). Low scores indicate high self-esteem, with the scores ranging from 10 to 40. The mean levels of self-esteem reported in the present study are much higher: liver transplant group, 19.3 (sd=6.6); liver control group, 19.8(sd=8.1); healthy control group 1, 16.9(sd=4.2); and healthy control group 2, 20.8(sd=4.0). The present

groups all demonstrate high self-esteem compared to the published norms. The reasons for these discrepancies are unclear, but perhaps reflect differences between North American and Scottish samples.

4.4.5. Transplant recipients will have a more positive acceptance of illness than chronically ill liver disease controls.

No difference between the two liver disease groups (Tr and LC) was found in their acceptance of illness scores (Table 15). Both groups' scores showed good acceptance of their illness, and were equivalent to published means with another chronic illness sample (Felton & Revenson, 1984). Although the transplant group could be considered no longer to be suffering from an illness (and indeed one subject did not fill in the questionnaire for this reason), many still report high levels of physical symptomatology (physical component of QoL scale), and all are taking high levels of medication, without which they would become very ill. It was predicted that the transplant group, given their successful transplant status, and the associated expected resumption of roles and activities, would have reported a better acceptance of illness. The fact that this was not the case indicates that there is not a shift in acceptance of the limitations of their health as expected.

4.4.6. Inadequate perceived social support will be associated with poorer quality of life and higher levels of anxiety and depression.

Again, no differences between the four groups (Tr, LC, HC1 and HC2) were found in actual or ideal, emotional and practical social support (Table 16). All groups were satisfied with the levels of emotional and practical social support they received. The high level of social support noted by transplant recipients in the present study supports findings by Leyendecker et al. (1993), who found that 80% of their sample of 45 liver transplant recipients reported having good social support. Another study found that

almost all of their sample of transplant recipients reported that family support was the most important factor in helping to cope with the post-transplantation period (Kuchler et al., 1991). The selection bias described in section 4.2. may in part explain the high levels of social support noted by both liver disease groups in the present study. The relationship between social support and health is unknown, and it may be that poor social support is related to higher levels of post-operative complications. Certainly, the adjustment to post-transplant changes, in particular the strict immunosuppressant medication regimens, would be difficult without good support from those around the individual. Many transplant recipients in the present sample reported the need for reminders and routines in their lives to help them cope with the pressure of drug regimens, frequent hospital appointments and constant fears of rejection and infections. Family and friends played an important role in facilitating these routines, and keeping the motivation going to keep to them. In contrast, another study found that, in an effort to maintain some control, the liver transplant recipients included in their study put themselves at risk by adjusting the times of their immunosuppressant medication (Thomas, 1993).

Across all groups in the present study, there were significant positive correlations between anxiety and discrepancy between actual and ideal, emotional and practical social support (Table 17). In other words, when actual emotional or practical support did not match up to ideals levels, the greater the anxiety reported. No significant correlations were found between social support and depression or QoL. The measure used to assess depression, the Hospital Anxiety and Depression Scale, is a fairly narrow measure of depression, and tends to focus on the symptom of anhedonia (Moorey et al., 1991). It may be that a more general measure of depression would be more likely to correlate with social support.

A study of supportive behaviours and sources of supportive behaviours in 20 pre-transplant adult patients with chronic liver disease, Geary et al. (1994) found that family was mentioned most as a social support. The types of supportive behaviour reported by patients included visits, telephone calls, prayers, cards, encouragement and chatting. A prospective study of these patients post-transplant, to investigate the role of social support further would be interesting. Wolcott et al. (1989) highlighted the discrepancy between large social networks but little social interaction experienced by their sample of liver transplant recipients. Their sample included a heterogeneous group of patients between 4 and 36 months post-transplant. It could be hypothesised that this discrepancy was more problematic the longer the time since transplantation, as health improves and recipients strive to regain social roles.

The importance of encouragement and support from family and friends was stressed by eight liver transplant recipients interviewed for a qualitative study designed to investigate the experience of liver transplantation (Wainwright, 1995). These recipients noted that social support was particularly important in the months following discharge from hospital, when the feelings of safety and security of being on the ward, with many nurses on hand, is lost. Further, the recovery process once at home can be slow, and physical limitations can remain for some time.

There is some evidence that support from fellow patients, either formally through support groups, or informally through friendships made while on the ward, can be very beneficial (Taylor, 1991; Moos & Schaefer, 1986). In fact, many patients report that they receive more information about the recovery trajectory of transplantation from other patients rather than from health professionals (Wainwright, 1995). Indeed the process of receiving support from other transplant recipients can follow a pattern in which each individual progresses to the role of supporting others, thus

reciprocating the support they had initially received. By three years post-operatively, however, the extent to which contact with other transplant recipients is beneficial is unclear. As time goes on, some transplant recipients report that they want to forget about their experiences of the transplant procedure and any difficulties they may have faced in the early stages after the transplant. It may be that the need for continued support from other transplant recipients reaches an end.

4.5. Qualitative Data: Problems Faced by Transplant Recipients

4.5.1. Waiting for the Transplant

The decision-making process that the transplant candidate goes through in deciding whether or not to have a transplant is complex. Some people cope better with a degree of choice and freedom, and others find this very stressful. The assessment procedure is lengthy and invasive, requiring transplant candidates to spend up to a week in hospital away from their homes. Liver transplant centres are regional, and there is only one in Scotland, based at the Royal Infirmary of Edinburgh. Patients from all over Scotland come to Edinburgh for assessment and, if considered suitable and if they agree, the transplantation procedure itself. Once it has been decided by all parties concerned that an individual should be placed on the waiting list for a liver transplant, they are sent home with a bleeper to wait for a suitable donor to become available. Up until the time the bleeper goes off, and the transplantation procedure is commenced, most transplant candidates have not considered fully the real impact that the transplant will have on their lives. Transplant recipients generally describe relief when the bleeper goes off, and it can be an emotional time as the prospect of death becomes imminent, when the individual says goodbye to family and friends (Wainwright, 1995).

4.5.2. Post-Transplant Adjustment

It was noted by a number of liver transplant recipients interviewed for this study that they were not prepared for the problems they experienced, particularly in the first year after their transplant. The initial euphoria, experienced when the realisation that the patient has survived the operation, can be short lived (Wainwright, 1995). Many of the transplant recipients described that they felt forgotten about by the transplant team once they had gone home after the transplant. Further, they find it very difficult to communicate fears and worries to the medical team. This is vital when it is considered that most transplant units do not routinely involve a psychologist, or other professional, who keeps in touch with the patients once they have been discharged. The only people that the patients see regularly are members of the medical team during out-patient appointments. Another factor that prevents patients acknowledging any fears, is that many of them have met and befriended other transplant candidates or recipients who have since been very ill and perhaps died during the transplant procedure or post-operatively. This can make the individual feel even more guilty about expressing difficulties, and can also highlight uncertainty about their own future.

The stresses and fears experienced post-operatively, once an individual has returned home, can be severe. Fear of rejection and infection can be intense, and many recipients report excessive symptom checking. Any infection the recipient picks up could jeopardise the health of their new livers, and therefore avoidance of places where infections may be picked up is understandable. This can be particularly difficult for parents of young children. In contrast, another study found that, in an effort to maintain some control, the liver transplant recipients they interviewed put themselves at risk by adjusting the times of their immunosuppressant medication and exposing themselves to situations that could increase their risk of infection (Thomas, 1993). This perhaps highlights the very

different experiences of liver transplantation faced by individual recipients. Anxiety symptoms can mimic more serious physical problems, for example racing heart, sweating, dry mouth, stomach churning and headaches. It could be concluded that this population of patients may benefit from the opportunity of access to psychological services, at the least to provide training in anxiety management techniques. The present sample did not show elevated levels of anxiety. Nevertheless, other researchers have noted that anxiety tends to peak in transplant recipients at times of crisis, for example during an infection (Kuchler et al., 1991). Further, the present sample were interviewed three years after their transplant, and most reported that by this stage they were coping much better, and with time the intensity of the fear of rejection and infection fades. It seems that the time when recipients are in most need of professional support is in the first year post-transplant. Indeed, Lowe et al. (1990) found that patients have more problems in the first year after a transplant that in the second or subsequent years. Survival through the first year post-transplant is seen as a significant hurdle both by patients and the medical team (Iwatsuki et al., 1987).

A major issue in the evaluation of the quality of life of transplant recipients is that individual differences must be considered. For example, a retired man, who has completed his working life and raised his family will have very different needs to a younger man who, prior to the development of chronic liver disease, had a manual job and was raising young children. The second man may need more input and advice from individuals to facilitate not just returning to work, but changing his profession. Many transplant recipients can be penalised by the employment services after receiving a successful transplant, as they are no longer considered "ill". A lack of understanding of the difficulties they face can be very upsetting and isolating. Levy et al. (1995) noted that some of their sample of liver transplant recipients had problems finding work or health insurance coverage (a particular problem in North American

samples), despite being healthy. The lack of advice on Social Security benefits, life assurance and job prospects was also highlighted as a major concern by the sample of liver transplant recipients interviewed by Wainwright (1995). A service providing advice, and liaising with other services, based in the transplant unit where these difficulties can be fully understood, should be available to transplant recipients.

The physical and psychological difficulties associated with chronic liver disease can result in the loss of roles, for example being able to care for your family, or being the main wage earner in the family. The reclaiming of these roles is an important aspect of an individuals' recovery from liver transplantation, as it provides individuals with a strong indication of improvement in their health. Failure to resume roles can be seen as evidence that illness is persisting (Johnson, 1991). Reclaiming former roles can, however, be difficult. Support from family and friends, which can be vital in the early stages post-operatively, can be perceived as over protection as the individual attempts to regain roles. In a group of women recovering from hysterectomy, it was found that family roles were harder to reclaim than roles at work and in the community (Chasse, 1991). Although liver transplant recipients may experience greater difficulties returning to work and reintegrating into the community than hysterectomy patients due to the nature of the surgery and the greater risk of complications, it may be that reintegration into family roles can be as difficult.

Despite the significant improvements in memory functioning of liver transplant recipients shown in the present study, it must be noted that a number of patients reported subjective complaints of memory problems. It may be that as health improves and roles are reclaimed, memory lapses become more noticeable. The old maxim, " use it or loose it", may be relevant here. Alternatively, it may be possible that transplant recipients are mislabelling 'normal' memory lapses as organic impairment

following the transplantation procedure. Similar findings were reported by Commander et al. (1992), who found that 40.6% of their sample of liver transplant recipients reported subjective memory problems.

4.6. Strengths of the Present Study

The present study has provided valuable information about the psychological sequelae of a relatively new health intervention. The prospective design, including three control groups and a holistic approach using standardised measures is in sharp contrast to the poorly designed majority of previous studies investigating neuropsychological and quality of life outcomes of liver transplantation. Results from the present study can therefore shed a realistic light on the experience and functioning of liver transplant recipients. Further, the present study attempted to overcome the risk of transplant recipients 'faking good' as it was carried out independently of the clinical contact with the transplant team, with the follow-up interview carried out at the patient's home when possible. In this way it was hoped that the liver transplant recipients included in the study would feel able to indicate any difficulties they were experiencing without guilt due to feelings of gratitude to the transplant team.

4.7. Weaknesses of the Present Study

Although the most obvious criticism is the inclusion of small sample sizes, it must be noted that the present study was carried out within strict time constraints, which limited the time available for the very lengthy process of follow-up assessment recruitment. This point is particularly relevant to transplant research given that most transplant centres are centralised, and patients attending the service can come from a wide geographical area. By three years post-transplant, most transplant recipients only visit the transplant unit at the Royal Infirmary of

Edinburgh once a year. For this study most follow-up assessments, therefore, needed to be carried out during home visits, which involved a great deal of travelling by the researcher.

It would be unethical to use a randomised, controlled trial design to investigate the psychological sequelae of liver transplantation. A chronic liver disease control group was included in the present study for comparison. The liver disease control group did not differ from the transplant group in terms of severity of liver disease at the initial recruitment stage or proportion of alcoholic cirrhotics included (Table 2) although the effects of immunosuppressant medication could not be controlled for (Reither et al., 1992).

The transplant recipients in the present study were limited to those who received their transplant due to chronic liver disease. A population of liver transplant recipients who received their transplant due to acute hepatic failure remain under-researched.

4.8. Factors that Mediate Successful Adjustment to Transplantation

Psychosocial adjustment to a prolonged life-threatening illness and major surgery, like liver transplantation, is shaped by numerous factors (Tarter et al., 1988c). The success of the transplantation procedure itself is one of these factors. This in turn is mediated by a number of variables. The chronicity of the underlying liver disease, the type of liver disease, concurrent illnesses, age, gender and grafting of the donor liver are all variables that will influence the success of the transplantation. Foley et al. (1989) found no correlation, however, between symptom frequency and associated distress and quality of life. Similarly, Leyendecker et al. (1993) found no relationship between low quality of life and transplant malfunction. Tarter et al. (1987b), however, found that psychosocial

adjustment to transplant was poorer for multiple transplant recipients rather than single transplant recipients. Only two out of the sixteen liver transplant recipients included in the present study had required a second liver transplant due to rejection of the first. Nevertheless, the variable of post-transplant complications was not included in the present study, and therefore remains a factor that requires further investigation.

4.9. WHAT THE PRESENT FINDINGS TELL US ABOUT LIVER TRANSPLANTATION

The present study provides rather different findings with regard to the psychological outcome of liver transplantation than those involved in the Scottish Liver Transplant Unit would have expected. In particular it was expected that quality of life would improve, and levels of anxiety and depression would decrease, in this group of transplant recipients 3 years post-transplant. Certainly, a literature review on the subject would lead the reader to believe that improvements in QoL are to be expected. Close inspection of the literature on this subject, however, reveals that it is rife with methodological flaws. Further, it may be that there is a selection bias in the type of study presented for publication given the pressure on transplant units to publish positive results. The present study is the first prospective, controlled study of its kind, evaluating neuropsychological functions, QoL and mood with standardised instruments 3 years post-transplant. Although small sample sizes limit the conclusions that can be drawn from the present study, it provides rather sobering evidence that the perceived benefits of liver transplantation in terms of QoL and mood are unrealistic. Nevertheless, there is clear evidence that mortality is reduced by the intervention of liver transplantation. That is, although QoL and mood did not improve 3 years post-transplant, the chance of death was significantly decreased (see section 3.1).

The conclusions that can be drawn from this evidence are perhaps most important in relation to the justification for transplantation. The

decision-making process involved in the assessment procedure can involve trade-offs between survival and QoL. A sample of those who receive a liver transplantation do so for purely QoL issues, before it is deemed a medical necessity. Patients may decide to have a liver transplant with the expectation that it will improve their QoL. The evidence provided in the present study perhaps casts doubt on whether liver transplants should be carried out for this reason. Despite survival benefits associated with transplantation, a transplant carried out before it is a medical necessity involves a degree of risk of premature death, whether on the operating table or due to post-operative complications. Further, if expectations about an improved QoL are not met, adjustment to living with a liver transplantation may be very difficult. Pre-operative counselling of patients assessed for liver transplantation, based on the empirical evidence of the present study, would have to highlight that QoL may not improve after the transplant and many difficulties may be faced. It remains to be seem whether this would influence the decision-making process of either the patient or the surgeons and physicians. It is interesting to note that there is now a body of literature recommending that QoL should be an important factor in the decision making process involved in the treatment of cancer (e.g. Reifel & Ganz, 1997). QoL has also been demonstrated to be a predictor of patient prognosis and response to treatment for metastatic lung cancer (Ganz et al., 1991). It may be that successful treatment of cancer can restore an individuals' QoL entirely in the sense that the individual can be completely 'cured'. Liver transplant recipients, on the other hand, may not feel 'cured' as they remain on a lifetime of immunosuppressant medication and carry with them the fear of rejection and infection. Further, transplant recipients' sense of themselves may be distorted by knowing that they have a new organ in their body. The support for this latter point is mixed and requires further investigation (Wainwright, 1995).

The significant improvements in memory functioning found in the present study, however, provide empirical evidence of the neuropsychological benefits of liver transplantation. The measure used in the present study to assess memory function (RBMT) was chosen because it was designed to detect impairment of everyday memory functioning and to monitor change over time. The items involve either remembering to carry out some everyday task, or retaining the type of information needed for adequate everyday functioning. It can therefore be concluded that the significant improvement on this measure would have a meaningful impact on the individuals' functioning in normal life. Further, there was no difference between scores on the RBMT between transplant recipients and well matched controls 3 years post-transplant, indicating that the intervention of liver transplantation normalises the memory functioning of recipients. Despite this, however, recipients in the present study were still complaining of memory problems. It may be that they need reassurance and reminding that a degree of memory lapses are normal experiences.

4.10. CONCLUSIONS

The present study is the first prospective, controlled study of QoL, mood and neuropsychological functioning in a sample of Scottish liver transplant recipients. The most striking results of the present study are the lack of improvements in the quality of life and mood of transplant recipients three years post-transplant, compared with pre-transplant levels. There was, however, a significant and meaningful improvement in the memory functioning of transplant recipients. Concerns over the rising cost of healthcare, and the need to justify expensive interventions such as liver transplantation, have focussed attention on psychological outcome measures. Nevertheless, the present study provides some evidence that the psychological needs of liver transplant recipients are not

always met. This has implications for the development of clinical psychology services as well as management of liver transplant units.

4.11. FUTURE RESEARCH

Research in this area has tended to be characterised by methodological flaws. Evidently there is a need for more prospective, controlled studies, with larger sample sizes investigating the psychological sequelae of liver transplantation. More specifically, a number of research questions remain to be investigated, for example:

1. Does psychological outcome of liver transplantation for acute liver failure differ from that for chronic liver failure?

2. Do interventions aimed at aiding adjustment to transplantation, e.g. support groups and anxiety management, improve quality of life and mood in transplant recipients?

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Appendix 1: Letter to patients

PSYCHOLOGY DEPARTMENT
Liver Transplant Unit
Royal Infirmary of Edinburgh

Dear

You may recall that we met previously when you were having treatment for liver disease at the Royal Infirmary of Edinburgh. I am currently contacting all those people with whom I had contact at that time. This is part of an evaluation of the longer term impact of liver disease and its' treatment.

I have included a number of questionnaires for you to complete, some of which you will have completed previously. A postage paid return envelope is also enclosed. However, I am also keen to meet with as many people face to face to discuss how you are getting on. This would either take place at the Royal Infirmary of Edinburgh at your own home, whichever is most convenient for you. I have enclosed a form for you to fill out indicating whether you would be prepared to meet with me or not. I would be very grateful if you could return this to me.

Please do not hesitate to contact me if you have any doubts or unanswered questions regarding this work.

I look forward to hearing from you.

Yours sincerely

Rebecca Gooday
Psycholigist

Appendix 2: Consent form

Dear Rebecca Gooday

Further to your letter I would like:

Please tick as appropriate.

No further contact ☐

To meet with you at the
Royal Infirmary of Edinburgh ☐

To meet with you at my home ☐

My telephone number is _____

Signed _____

Appendix 3: Rotterdam Symptom Checklist

ROTTERDAM SYMPTOM CHECKLIST (CORE)

Patient's Name:	Date of Assessment: .....
Transplant Status:	Other: .....

In this questionnaire you will be asked about your symptoms. Against each item place a firm tick under the heading that best describes how you have been feeling during the past week.

	Not at all	A little	Moderately	Very much
1. Lack of appetite				
2. Irritability				
3. Tiredness				
4. Worrying				
5. Sore muscles				
6. Depressed mood				
7. General pain				
8 Nervousness				
9. Nausea				
10. Despondent or desperate feelings about the future				
11. Difficulty sleeping				
12. Headaches				
13. Dizziness				
14. Sore stomach				
15. Decreased sexual interest				
16. Feeling tense				
17. Anxious feelings				
18. Heartburn/acidity				
19. Tingling of hands or feet				
20. Difficulty concentrating				
21. Concern about jaundice				
22. Itching				
23. Lack of energy				
24. Shortness of breath				
25. Dry mouth				
26. Shivering				
27. Feeling bloated				

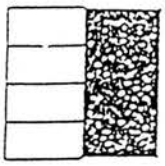
Appendix 4: Hospital Anxiety and Depression Scale

HAD SCALE Date..... ID No. .....

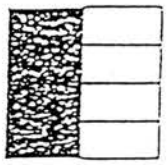
Read each item and place a tick in the box opposite the reply which comes closest to how you have been feeling in the past week.

Don't take too long over your replies: your immediate reaction to each item will probably be more accurate than a long thought-out response.

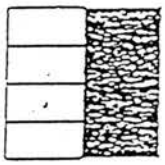
feel tense or 'wound up':
- Most of the time .....
- A lot of the time .....
- Time to time, Occasionally .....
- Not at all .....



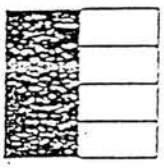
still enjoy the things I used to enjoy:
- Definitely as much .....
- Not quite so much .....
- Only a little .....
- Hardly at all .....



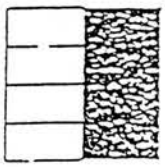
get a sort of frightened feeling as if omething awful is about to happen:
- Very definitely and quite badly .....
- Yes, but not too badly .....
- A little, but it doesn't worry me .....
- Not at all .....



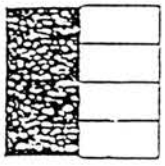
can laugh and see the funny side of ings:
- As much as I always could .....
- Not quite so much now .....
- Definitely not so much now .....
- Not at all .....



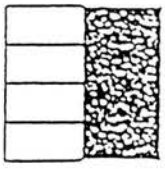
orrying thoughts go through my nd:
- A great deal of the time .....
- A lot of the time .....
- From time to time but not too often ..
- Only occasionally .....



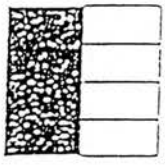
eel cheerful:
- Not at all .....
- Not often .....
- Sometimes .....
- Most of the time .....



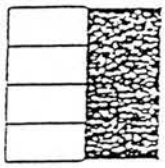
an sit at ease and feel relaxed:
- Definitely .....
- Usually .....
- Not often .....
- Not at all .....



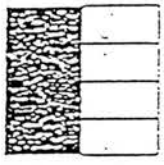
I feel as if I am slowed down:
- Nearly all the time .....
- Very often .....
- Sometimes .....
- Not at all .....



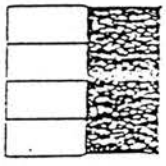
I get a sort of frightened feeling like 'butterflies' in the stomach:
- Not at all .....
- Occasionally .....
- Quite often .....
- Very often .....



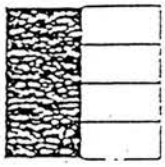
I have lost interest in my appearance:
- Definitely .....
- I don't take so much care as I should.....
- I may not take quite as much care .....
- I take just as much care as ever .....



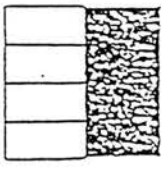
I feel restless as if I have to be on the move:
- Very much indeed .....
- Quite a lot .....
- Not very much .....
- Not at all .....



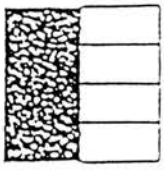
I look forward with enjoyment to things:
- As much as ever I did .....
- Rather less than I used to .....
- Definitely less than I used to .....
- Hardly at all .....



I get sudden feelings of panic:
- Very often indeed .....
- Quite often .....
- Not very often .....
- Not at all .....



I can enjoy a good book or radio or TV programme:
- Often .....
- Sometimes .....
- Not often .....
- Very seldom .....



Appendix 5: Rosenberg Self-Esteem Scale

ROSENBERG SELF-ESTEEM SCALE

Name: .....

Date: ..... **Record Number:** .....

Here is a list of statements dealing with your general feelings about yourself. If you **agree** with the statement, circle A. If you **strongly agree**, circle SA. If you **disagree**, circle D. If you **strongly disagree**, circle SD. Thank you.

	1 Strongly agree	2 Agree	3 Disagree	4 Strongly disagree
1. On the whole, I am satisfied with myself.	SA	A	D	SD
2. At times I think I am no good at all.	SA	A	D	SD
3. I feel that I have a number of good qualities.	SA	A	D	SD
4. I am able to do things as well as most other people.	SA	A	D	SD
5. I feel I do not have much to be proud of.	SA	A	D	SD
6. I certainly feel useless at times.	SA	A	D	SD
7. I feel that I'm a person of worth, at least on an equal plane with others.	SA	A	D	SD
8. I wish I could have more respect for myself.	SA	A	D	SD
9. All in all, I am inclined to feel that I am a failure.	SA	A	D	SD
10. I take a positive attitude toward myself.	SA	A	D	SD

Appendix 6: Acceptance of Illness Scale

ACCEPTANCE OF ILLNESS SCALE

Name: .....

Date: ..... **Record Number:** .....

Instructions

Please respond to each of the following items by choosing a number from 1 to 5 on the scale adjacent to the item which you feel best describes you. Then **circle** the number you have chosen. There are no right answers to any of the questions.

1. I have a hard time adjusting to the limitations of my illness.

Strongly agree	1	2	3	4	5	Strongly disagree

2. Because of my health, I miss the things I like to do most.

Strongly agree	1	2	3	4	5	Strongly disagree

3. My illness makes me feel useless at times.

Strongly agree	1	2	3	4	5	Strongly disagree

4. Health problems make me more dependent on others than I want to be.

Strongly agree	1	2	3	4	5	Strongly disagree

5. My illness makes me a burden on my family and friends.

Strongly agree	1	2	3	4	5	Strongly disagree

6. My health does not make me feel inadequate.

Strongly agree	1	2	3	4	5	Strongly disagree

7. I will never be self-sufficient enough to make me happy.

Strongly agree	1	2	3	4	5	Strongly disagree

8. I think people are often uncomfortable being around me because of my illness.

Strongly agree	1	2	3	4	5	Strongly disagree

Appendix 7: Significant Others Scale

SIGNIFICANT OTHERS SCALE (B)

Name: .....

Date: ..... **Record Number:** .....

Instructions

Please list below **up to seven people** who may be important in the individual's life. Typical relationships include partner, mother, father, child, sibling, close friends, plus keyworker. For each person please circle a number from 1 to 7 to show how well he or she provides the type of help that is listed.

The second part of each question asks you to rate how individuals would like things to be if they were exactly as they hoped for. As before, please put a circle around one number between 1 and 7 to show what the rating is.

Person 1 –	*Never*			*Sometimes*			*Always*
1 a) Can you trust, talk to frankly and share your feelings with this person?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
2 a) Can you lean on and turn to this person in times of difficulty? ..	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
3 a) Does he/she give you practical help?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
4 a) Can you spend time with him/her socially?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
Person 2 –							
1 a) Can you trust, talk to frankly and share your feelings with this person?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
2 a) Can you lean on and turn to this person in times of difficulty? ..	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
3 a) Does he/she give you practical help?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
4 a) Can you spend time with him/her socially?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
Person 3 –							
1 a) Can you trust, talk to frankly and share your feelings with this person?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
2 a) Can you lean on and turn to this person in times of difficulty?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
3 a) Does he/she give you practical help?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
4 a) Can you spend time with him/her socially?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7

PLEASE CIRCLE ONE NUMBER ONLY FOR EACH QUESTION

Person 4 –	*Never*			*Sometimes*			*Always*
1 a) Can you trust, talk to frankly and share your feelings with this person?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
2 a) Can you lean on and turn to this person in times of difficulty?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
3 a) Does he/she give you practical help?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
4 a) Can you spend time with him/her socially?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7

Person 5 –							
1 a) Can you trust, talk to frankly and share your feelings with this person?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
2 a) Can you lean on and turn to this person in times of difficulty?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
3 a) Does he/she give you practical help?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
4 a) Can you spend time with him/her socially?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7

Person 6 –							
1 a) Can you trust, talk to frankly and share your feelings with this person?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
2 a) Can you lean on and turn to this person in times of difficulty?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
3 a) Does he/she give you practical help?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
4 a) Can you spend time with him/her socially?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7

Person 7 –							
1 a) Can you trust, talk to frankly and share your feelings with this person?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
2 a) Can you lean on and turn to this person in times of difficulty?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
3 a) Does he/she give you practical help?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7
4 a) Can you spend time with him/her socially?	1	2	3	4	5	6	7
b) What rating would your ideal be?	1	2	3	4	5	6	7

PLEASE CIRCLE ONE NUMBER ONLY FOR EACH QUESTION